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L18	L17 and emulsion adj5 liposome adj5 adjuvant	4	L18
L17	L16 and adjuvant	6797	L17
L16	L15 and antigen	8882	L16
L15	emulsion and liposome	15389	L15
L14	emulsion	340887	L14
L13	L12 and zona pellucida	39	L13
L12	L11 and (alum or aluminum)	2718	L12
L11	L10 and adjuvant	4789	L11
L10	L9 and liposom?	6068	L10
L9	emulsion and antigen	17016	L9
L8	emulsion adj5 liposom? adj5 antigen adj5 adjuvant	0	L8
L7	L6 and adjuvant	4	L7
L6	l1 or l2 or l3 or l4	13	L6
L5	kimmins-warwick.in.	0	L5
L4	kimmins-warwick-charles.in.	4	L4
L3	kimmins-warwick-charles.in	0	L3
L2	pohajdak-bill.in.	6	L2
L1	brown-robert-george.in.	7	L1

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9/992149

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               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
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E2            1     BROWN ROBERT GENE/AU
E3            6 --> BROWN ROBERT GEORGE/AU
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E6            4      BROWN ROBERT GRAVES/AU
E7            2      BROWN ROBERT GWYN/AU
E8          136      BROWN ROBERT H/AU
E9          145      BROWN ROBERT H JR/AU
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E11           8      BROWN ROBERT HAMILTON/AU
E12           1      BROWN ROBERT HAROLD/AU

=> s e3
L1            6 "BROWN ROBERT GEORGE"/AU

=> e brown r g/au
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E6            2      POHALA M J/AU
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L3          211 ("POHAJDAK B"/AU OR "POHAJDAK BILL"/AU OR "POHAJDAK W"/AU OR
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=> s l1-l5
L6        1222 (L1 OR L2 OR L3 OR L4 OR L5)

=> s l6 and adjuvant
L7           9 L6 AND ADJUVANT

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8           5 DUP REM L7 (4 DUPLICATES REMOVED)

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     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS' ENTERED AT 10:30:55 ON 24 JUN 2003
               E BROWN ROBERT GEORGE/AU
L1             6 S E3
               E BROWN R G/AU
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L3           211 S E2-E5
               E KIMMINS WARWICK CHARLES/AU
L4            14 S E1-E3
               E KIMMINS W C/AU
L5           115 S E2-E6
L6          1222 S L1-L5
L7             9 S L6 AND ADJUVANT
L8             5 DUP REM L7 (4 DUPLICATES REMOVED)

=> d bib ab 1-5
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L8 ANSWER 1 OF 5 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 1
AN 2002-454763 [48] WPIDS
DNC C2002-129354
TI Composition useful as vaccine comprises carrier, liposome, antigen and **adjuvant**.
DC B04 C03 D16
IN **BROWN, R G**; **KIMMINS, W C**; **POHAJDAK, W**
PA (BROW-I) BROWN R G; (KIMM-I) KIMMINS W C; (POHA-I) POHAJDAK W; (IMMU-N) IMMUNOVACCINE TECHNOLOGIES INC
CYC 98

PI WO 2002038175 A1 20020516 (200248)* EN 66p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002110568 A1 20020815 (200256)
AU 2002014861 A 20020521 (200260)
ADT WO 2002038175 A1 WO 2001-CA1530 20011031; US 2002110568 A1 Provisional US 2000-246075P 20001107, Provisional US 2001-307159P 20010724, US 2001-992149 20011106; AU 2002014861 A AU 2002-14861 20011031
FDT AU 2002014861 A Based on WO 200238175
PRAI US 2001-307159P 20010724; US 2000-246075P 20001107; US 2001-992149 20011106
AB WO 200238175 A UPAB: 20020730
NOVELTY - A composition (I) comprises a carrier (C), liposomes, an antigen and an **adjuvant** (A). (C) comprises a continuous phase of hydrophobic substance.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the following:
(1) preparing (I) involving:
(a) encapsulating an antigen or an antigen/**adjuvant** complex in liposomes to form liposome-encapsulated antigen;
(b) mixing the liposome-encapsulated antigen with (C), and
(c) optionally adding (A) if antigen/**adjuvant** complex is not used in step (a).
USE - As a vaccine composition (claimed).
ADVANTAGE - The composition provides effective long-term immunocontraception in a mammal. The composition is free of lipid A. The composition potentiates and enhances an immune response in an animal. A single dose of the composition provides long-term immune response in a variety of species, typically not requiring boosters. The antigen used elicits an antibody that recognizes a native epitope in mammals such as horse, rabbit, deer and cat.
Dwg.0/1

L8 ANSWER 2 OF 5 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2003) DUPLICATE 2
AN 2003:15636 AGRICOLA
DN IND23308151
TI Evaluation of a porcine zona pellucida vaccine for the immunocontraception of domestic kittens (Felis catus).
AU Gorman, S.P.; Levy, J.K.; Hampton, A.L.; Collante, W.R.; Harris, A.L.; **Brown, R.G.**
AV DNAL (QP251.A1T5)
SO Theriogenology, July 1, 2002. Vol. 58, No. 1. p. 135-149
Publisher: New York, N.Y. : Elsevier Science Inc.
CODEN: THGNBO; ISSN: 0093-691X
NTE Includes references
CY New York (State); United States
DT Article
FS U.S. Imprints not USDA, Experiment or Extension
LA English
AB With a seasonally polyestrus breeding structure, the unwanted domestic cat population has proven difficult to control. Various lethal methods have been used in an attempt to lower this population of cats. Recently, humane attempts to control "pest species," such as the feral cat, have focused on immunocontraception. SpayVac is a vaccine that uses antibodies raised against porcine (ZP) antigens to prevent fertilization of the ovum. SpayVac, delivered in a single dose, has been evaluated in fallow deer and

several species of seals with greater than or equal to 90% reduction in fertility and no adverse reactions. This study evaluated the effectiveness of SpayVac in reducing fertility in domestic kittens. Thirty female kittens were treated with SpayVac containing either Freund's complete **adjuvant** (FCA) or alum, or with a control vehicle. Kittens were monitored for side effects, estrus cycling at maturity, and fecundity. Anti-porcine ZP antibodies were quantified by ELISA. Immunohistochemical assays measured the species specificity of the antibodies produced and IgG binding in vivo. Despite high anti-porcine ZP antibody titers, neither formulation of SpayVac prevented estrus cycling at maturity or reduced fecundity. Immunohistochemical assays indicated that antibodies produced by cats treated with SpayVac recognized porcine ZP, but not feline ZP.

L8 ANSWER 3 OF 5 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-442535 [38] WPIDS
DNC C2000-134656
TI Contraceptive vaccines for fish and birds, useful e.g. for preventing breeding of escaped transgenic fish, contains teleost homolog of zona pellucida or antigen from inner perivitelline layer.
DC B04 C06 D16
IN BROWN, R; HORROCKS, J; **KIMMINS, W C**; MACLAREN, L; **POHAJDAK, B**
PA (UYDA-N) UNIV DALHOUSIE
CYC 91
PI WO 2000037100 A2 20000629 (200038)* EN 44p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000017653 A 20000712 (200048)
EP 1140151 A2 20011010 (200167) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000037100 A2 WO 1999-CA1225 19991222; AU 2000017653 A AU 2000-17653 19991222; EP 1140151 A2 EP 1999-960753 19991222, WO 1999-CA1225 19991222
FDT AU 2000017653 A Based on WO 200037100; EP 1140151 A2 Based on WO 200037100
PRAI US 1998-113526P 19981222
AB WO 200037100 A UPAB: 20000811
NOVELTY - Immunocontraceptive vaccine (A) comprises a teleost homolog of zona pellucida (TH-ZP) and a diluent or carrier, for reducing or preventing fertilization of fish.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for reducing or preventing fertilization of fish by administration of (A);

(2) an immunocontraceptive vaccine (B) comprising an antigen (Ag) from the inner perivitelline layer (IPVL) of a bird and a carrier or diluent, for reducing or preventing fertilization in birds; and

(3) a method for reducing or preventing fertilization of birds by administration of (B).

ACTIVITY - Contraceptive.

MECHANISM OF ACTION - Vaccine.

USE - (A) is used to reduce or prevent fertility in fish, and a similar vaccine (B) based on an antigen of the inner perivitelline layer is used correspondingly in birds. Applications include:

(i) sterilizing farmed transgenic fish (particularly rainbow trout) so that they can not breed if they escape into the wild; and

(ii) control of populations of birds that cause economic losses or damage fragile environments by overgrazing, e.g. the snow goose (Chen caerulescens) on tundra.

ADVANTAGE - The vaccines are effective after a single injection,

particularly when formulated as liposomes for slow release of the immunologically active component.
Dwg.0/4

L8 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:107111 BIOSIS
DN PREV200200107111
TI Method to prevent fertilization in mammals by administering a single dose of zona pellucida derived antigens, liposome and Freund's **adjuvant**.
AU Brown, R.; Mezei, M.; **Pohajdak, B.**; **Kimmins, W. C.**
CS Dartmouth Canada
ASSIGNEE: DALHOUSIE UNIVERSITY
PI US 5736141 April 7, 1998
SO Official Gazette of the United States Patent and Trademark Office Patents, (April 7, 1998) Vol. 1209, No. 1, pp. 399.
ISSN: 0098-1133.
DT Patent
LA English

L8 ANSWER 5 OF 5 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 3
AN 1994-007198 [01] WPIDS
DNC C1994-002812
TI Immuno contraception of mammals, partic. rabbits and seals - using zona pellucida derived antigen incorporated into liposome system.
DC B04 C06 D16
IN BROWN, R; **KIMMINS, W C**; MEZEI, M; **POHAJDAK, B**; **KIMMINS, W**
PA (UYDA-N) UNIV DALHOUSIE
CYC 43
PI WO 9325231 A1 19931223 (199401)* EN 26p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US VN
AU 9343034 A 19940104 (199417)
US 5736141 A 19980407 (199821) 7p
CA 2137363 C 19990615 (199942) EN
US 37224 E 20010612 (200135)
ADT WO 9325231 A1 WO 1993-CA239 19930607; AU 9343034 A AU 1993-43034 19930607; US 5736141 A CIP of US 1992-892807 19920605, Cont of WO 1993-CA239 19930607, Cont of US 1994-347348 19941205, US 1996-739812 19961030; CA 2137363 C CA 1993-2137363 19930607, WO 1993-CA239 19930607; US 37224 E CIP of US 1992-892807 19920605, Cont of WO 1993-CA239 19930607, Cont of US 1994-347348 19941205, US 1996-739812 19961030, US 1998-156159 19980723
FDT AU 9343034 A Based on WO 9325231; CA 2137363 C Based on WO 9323231; US 37224 E Reissue of US 5736141
PRAI US 1992-892807 19920605; US 1994-347348 19941205; US 1996-739812 19961030; US 1998-156159 19980723
AB WO 9325231 A UPAB: 20010716
Vaccine compsn. comprises a zona pellucida(ZP) derived antigen incorporated into a liposome system. Zona ellucida antigen is pref. ZP3 and compsn. may also include an **adjuvant**, e.g. Freund's **adjuvant**.

Also claimed is a compsn. capable of inducing the prodn. of antibodies to a ZP antigen, the compsn. comprising a ZP-derived antigen incorporated into a liposome system.

USE/ADVANTAGE - For preventing fertilisation in mammals, partic. domestic and wild animals e.g. rabbits and seals. Liposome system effects the slow release of antigen resulting in an extended period of antibody prodn., hence an extended period of contraception.

In an example, rabbits were injected with porcine solubilised intact ZP glycoprotins (SIZP, 20g) encapsulated in liposomes contg. phospholipon 904 (RTM, 0.1g) cholesterol (0.1g) and saline (0.25 ml) and FCA (0.25 ml).

Liposomes were prepd. as in US4,485,054 and single injection was used. Measurement of antibodies directed specifically against ZP3 indicated than antibodies were produced by day 27 and antibody prodn. remained high at day 69.
Dwg.0/0

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L3          211 S E2-E5
                E KIMMINS WARWICK CHARLES/AU
L4           14 S E1-E3
                E KIMMINS W C/AU
L5          115 S E2-E6
L6         1222 S L1-L5
L7            9 S L6 AND ADJUVANT
L8            5 DUP REM L7 (4 DUPLICATES REMOVED)

=> s l7 and liposom?
L9            7 L7 AND LIPOSOM?

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10           4 DUP REM L9 (3 DUPLICATES REMOVED)

=> d bib 1-4

L10  ANSWER 1 OF 4  WPIDS (C) 2003 THOMSON DERWENT     DUPLICATE 1
AN   2002-454763 [48]   WPIDS
DNC  C2002-129354
TI   Composition useful as vaccine comprises carrier, liposome,
     antigen and adjuvant.
DC   B04 C03 D16
IN   BROWN, R G; KIMMINS, W C; POHAJDAK, W
PA   (BROW-I) BROWN R G; (KIMM-I) KIMMINS W C; (POHA-I) POHAJDAK W; (IMMU-N)
     IMMUNOVACCINE TECHNOLOGIES INC
CYC  98
PI   WO 2002038175 A1 20020516 (200248)* EN   66p
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            RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
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     AU 2002014861 A  20020521 (200260)
ADT  WO 2002038175 A1 WO 2001-CA1530 20011031; US 2002110568 A1 Provisional US
     2000-246075P 20001107, Provisional US 2001-307159P 20010724, US
     2001-992149 20011106; AU 2002014861 A AU 2002-14861 20011031
FDT  AU 2002014861 A Based on WO 200238175
PRAI US 2001-307159P  20010724; US 2000-246075P  20001107; US 2001-992149
     20011106

L10  ANSWER 2 OF 4  WPIDS (C) 2003 THOMSON DERWENT
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AN 2000-442535 [38] WPIDS
DNC C2000-134656
TI Contraceptive vaccines for fish and birds, useful e.g. for preventing breeding of escaped transgenic fish, contains teleost homolog of zona pellucida or antigen from inner perivitelline layer.
DC B04 C06 D16
IN BROWN, R; HORROCKS, J; **KIMMINS, W C**; MACLAREN, L; **POHAJDAK, B**
PA (UYDA-N) UNIV DALHOUSIE
CYC 91
PI WO 2000037100 A2 20000629 (200038)* EN 44p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000017653 A 20000712 (200048)
EP 1140151 A2 20011010 (200167) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000037100 A2 WO 1999-CA1225 19991222; AU 2000017653 A AU 2000-17653 19991222; EP 1140151 A2 EP 1999-960753 19991222, WO 1999-CA1225 19991222
FDT AU 2000017653 A Based on WO 200037100; EP 1140151 A2 Based on WO 200037100
PRAI US 1998-113526P 19981222

L10 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:107111 BIOSIS
DN PREV200200107111
TI Method to prevent fertilization in mammals by administering a single dose of zona pellucida derived antigens, **liposome** and Freund's **adjuvant**.
AU Brown, R.; Mezei, M.; **Pohajdak, B.**; **Kimmins, W. C.**
CS Dartmouth Canada
ASSIGNEE: DALHOUSIE UNIVERSITY
PI US 5736141 April 7, 1998
SO Official Gazette of the United States Patent and Trademark Office Patents, (April 7, 1998) Vol. 1209, No. 1, pp. 399.
ISSN: 0098-1133.
DT Patent
LA English

L10 ANSWER 4 OF 4 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 2
AN 1994-007198 [01] WPIDS
DNC C1994-002812
TI Immuno contraception of mammals, partic. rabbits and seals - using zona pellucida derived antigen incorporated into **liposome** system.
DC B04 C06 D16
IN BROWN, R; **KIMMINS, W C**; MEZEI, M; **POHAJDAK, B**; **KIMMINS, W**
PA (UYDA-N) UNIV DALHOUSIE
CYC 43
PI WO 9325231 A1 19931223 (199401)* EN 26p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US VN
AU 9343034 A 19940104 (199417)
US 5736141 A 19980407 (199821) 7p
CA 2137363 C 19990615 (199942) EN
US 37224 E 20010612 (200135)
ADT WO 9325231 A1 WO 1993-CA239 19930607; AU 9343034 A AU 1993-43034 19930607; US 5736141 A CIP of US 1992-892807 19920605, Cont of WO 1993-CA239 19930607, Cont of US 1994-347348 19941205, US 1996-739812 19961030; CA

2137363 C CA 1993-2137363 19930607, WO 1993-CA239 19930607; US 37224 E CIP of US 1992-892807 19920605, Cont of WO 1993-CA239 19930607, Cont of US 1994-347348 19941205, US 1996-739812 19961030, US 1998-156159 19980723
FDT AU 9343034 A Based on WO 9325231; CA 2137363 C Based on WO 9323231; US 37224 E Reissue of US 5736141
PRAI US 1992-892807 19920605; US 1994-347348 19941205; US 1996-739812 19961030; US 1998-156159 19980723

=> s liposom? (5a) emulsion (5a) antigen (5a) adjuvant
L11 2 LIPOSOM? (5A) EMULSION (5A) ANTIGEN (5A) ADJUVANT

=> d bib ab 1-2

L11 ANSWER 1 OF 2 LIFESCI COPYRIGHT 2003 CSA
AN 1999:44892 LIFESCI
TI Vaccine compositions containing liposomes
AU Barchfeld, G.L.; Ott, G.; Van Nest, G.A.
CS Chiron Corporation
SO (19980120) . US Patent 5709879; US Class: 424/450; 424/184.1; 424/204.1; 424/234.1; 424/812; 514/2; 514/937; 514/938..
DT Patent
FS W3
LA English
SL English
AB A vaccine composition, comprising an antigenic substance in association with a liposome and an oil-in-water emulsion comprising a muramyl peptide, a metabolizable oil, and optionally an additional emulsifying agent. The two components of the **adjuvant** (i.e., the **liposome/antigen** component and the **emulsion** component) act together to produce high levels of immune response.

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 2002:346583 CAPLUS
DN 138:95279
TI Liposomes and emulsions as adjuvants for immunization: Mechanisms for amplification of immune effectors through controlled release
AU Alving, Carl R.; Rao, Mangala; Matyas, Gary R.
CS Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Silver Spring, MD, 20910-7500, USA
SO Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 1, 12-13 Publisher: Controlled Release Society, Minneapolis, Minn. CODEN: 69CNY8
DT Conference; General Review
LA English
AB A review discussing mechanisms of controlled-release of antigen for immunization by antigen-encapsulated liposomes in relation to interaction with antigen presenting cell (APC), and utilization of adjuvants contg. liposome-stabilized emulsions. In addn. to the class II pathway, the authors have discovered that a large amt. of liposomal antigen is also released into the cytoplasm of the APC where it is degraded to lipopeptides and delivered to the Golgi complex. Subsequent studies with liposome-stabilized emulsions have demonstrated that this formulation shows considerable promise for creating vaccines against liposome-encapsulated viral antigens and tumor antigens.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s liposom? and antigen
L12 8577 LIPOSOM? AND ANTIGEN

=> s l12 and adjuvant
L13 1436 L12 AND ADJUVANT

=> s l13 and emuslion (10a) carrier
L14 0 L13 AND EMUSLION (10A) CARRIER

=> s l13 and emulsion
L15 96 L13 AND EMULSION

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16 61 DUP REM L15 (35 DUPLICATES REMOVED)

=> s l16 and carrier
L17 18 L16 AND CARRIER

=> d bib ab 1-18

L17 ANSWER 1 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1984:226460 BIOSIS
DN BA77:59444
TI ORAL ADJUVANTS ENHANCE IMMUNO GLOBULIN A RESPONSES TO STREPTOCOCCUS-MUTANS.
AU MICHALEK S M; MORISAKI I; GREGORY R L; KIYONO H; HAMADA S; MCGHEE J R
CS DEP. MICROBIOL., INST. DENT. RES., UNIV. ALABAMA BIRMINGHAM, UNIV. STN., BIRMINGHAM, ALA. 35294, USA.
SO MOL IMMUNOL, (1983) 20 (9), 1009-1018.
CODEN: MOIMD5. ISSN: 0161-5890.
FS BA; OLD
LA English
AB The induction of immune responses to orally-administered trinitrophenyl (TNP)-haptenated S. mutans or its cell wall components and enhancement of immune responses with oral adjuvants was studied in high IgA responsive C3H/HeJ mice and in gnotobiotic rats. Gastric intubation of TNP-S. mutans to LPS [lipopolysaccharide] non-responsive C3H/HeJ or syngeneic, LPS responsive C3H/HeN mice induced IgA responses as determined by measuring splenic plaque-forming cell (PFC) responses and IgA anti-TNP antibodies in serum, saliva and urine. Higher IgA responses always occurred in C3H/HeJ mice given oral S. mutans **antigen** than similarly treated C3H/HeN animals. Oral administration of the adjuvants concanavalin A or S. mutans cell wall peptidoglycan (PG) with **antigen** resulted in augmented IgA responses, especially in C3H/HeJ mice. Oral administration of muramyl dipeptide (MDP) with **antigen** boosted anti-TNP responses in C3H/HeN, but not in C3H/HeJ, mice. Gnotobiotic rats given S. mutans whole cells (WC) or purified cell walls (CW) by the oral route exhibited a salivary IgA immune response which was potentiated > 2-fold when **antigen** was given with PG or MDP. In other studies, S. mutans WC or CW **antigen** in water-oil-water (wow) **emulsion** or **liposomes** was administered by gastric intubation to rats. Significant salivary IgA responses were induced with these **antigen** -**adjuvant** preparations. Although rats given S. mutans WC or CW were protected from S. mutans challenge, the greatest degree of caries immunity was obtained in animals which received **antigen** and **adjuvant** and which exhibited significant salivary IgA antibody levels. In preliminary studies, it was observed that local injection of rats in the salivary gland region with a ribosomal preparation from S. mutans resulted in a significant salivary IgA response and caries immunity. The potential for soluble and lipid **carrier** adjuvants in oral vaccines for induction of protective antibodies to S. mutans is discussed.

L17 ANSWER 2 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 2001428649 EMBASE
TI [Vaccines and vaccine adjuvants].
ASILAR VE ASI ADJUVANLAN.
AU Eratalay A.; Oner F.
CS A. Eratalay, Hacettepe Universitesi, Eczacilik Fakultesi, Farmasotik Biyoteknoloji Anabilim, Ankara, Turkey
SO Fabad Journal of Pharmaceutical Sciences, (2001) 26/1 (21-33).
Refs: 99
ISSN: 1300-4182 CODEN: FBDEDQ
CY Turkey
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LA Turkish
SL English; Turkish
AB New vaccines have some advantages due to their purity and safety characteristics, over conventional vaccines, but preventive properties need to be progressed. This can be achieved by using some materials or carriers called adjuvants which helps to increase immune response to an **antigen**. There are two **adjuvant** formulations which have been used since 1950's. One of them is mineral oil emulsions including micobacteria or not, second one is gel or suspension formulations of aluminium salts. Studies on new adjuvants or **adjuvant** carriers are increasing due to the side effects of conventional adjuvants. Recently new adjuvants and **carrier** systems for modern vaccines are attracting more attention because of the poor immunogenicity of pure subunit or synthetic recombinant antigens and problems with aluminium based adjuvants. New adjuvants have to be nontoxic, noncarcinogenic, must not cause local and systemic reactions and they have to provide long term immune protection with small number of application. In this article **adjuvant carrier** systems and materials used for subunit and recombinant DNA derived vaccines are reviewed.

L17 ANSWER 3 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1999410119 EMBASE
TI **Liposomes** and emulsions as carriers of vaccines.
AU Alving C.R.; Matyas G.R.; Muderhwa J.M.; Spitler L.E.
CS C.R. Alving, Department of Membrane Biochemistry, Walter Reed Army Institute Research, Washington, DC 20307-5100, United States
SO Proceedings of the Controlled Release Society, (1999) -/26 (85-86).
Refs: 15
ISSN: 1022-0178 CODEN: 58GMAH
CY United States
DT Journal; Conference Article
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
038 Adverse Reactions Titles
LA English

L17 ANSWER 4 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 96280436 EMBASE
DN 1996280436
TI Immunological adjuvants: Mechanisms of action and clinical applications.
AU Sheikh N.; Rajananthanan P.; Morrow W.J.W.
CS Department of Immunology, St Bartholomew's/Royal London, School of Medicine/Dentistry, 38 Little Britain,London EC1A 7BE, United Kingdom
SO Expert Opinion on Investigational Drugs, (1996) 5/9 (1079-1099).
ISSN: 1354-3784 CODEN: EOIDER
CY United Kingdom

DT Journal; General Review
FS 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Adjuvants are a neglected aspect of vaccine formulations, prudent choice of which can enhance the immune response both quantitatively and qualitatively. This review details the evolution and current range of adjuvants, particularly those in clinical trials. The components of different adjuvants are outlined and the manner in which they are thought to work is discussed. **Antigen** processing is an essential requirement of any immune response and these mechanisms are discussed in the context of **adjuvant** action.

L17 ANSWER 5 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2003-402921 [38] WPIDS
DNN N2003-321461 DNC C2003-107147
TI Composition useful for enhancing the immunogenicity of veterinary vaccine comprises an immunomodulator and an immunoadjuvant.
DC A96 B04 C06 D16 P32
IN CHU, H
PA (AMHP) WYETH
CYC 100
PI WO 2003024354 A2 20030327 (200338)* EN 21p
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
ADT WO 2003024354 A2 WO 2002-US29229 20020913
PRAI US 2002-243075 20020912; US 2001-322840P 20010917
AB WO2003024354 A UPAB: 20030616
NOVELTY - A composition (C1) comprising an immunomodulator and an immunoadjuvant, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for an improved veterinary vaccine composition (C2) comprising an **antigen**, an immunomodulator, an immunoadjuvant and a **carrier**.
ACTIVITY - None given.
MECHANISM OF ACTION - Vaccine.
No biological data given.
USE - The composition is useful for enhancing the immunogenicity of a veterinary vaccine; for potentiating, accelerating or extending the immunogenicity of a weak, immunosuppressive or marginally safe **antigen** (all claimed).
ADVANTAGE - The composition improves the immunological response of an animal to the **antigen** when administered concurrently or in admixture with vaccine composition. The composition improves the immunogenicity and efficacy of animal vaccines without raising toxicity concerns. The composition provides highly unique vaccine possessing significantly improved immunogenicity in mammals and birds by inducing a stronger stimulation on cell-mediated immunity including T memory cells and to provide a longer duration of immunity by requiring smaller or less frequent dosages of antigens over time and lessening side effects or potential for toxicity.
Dwg.0/0

L17 ANSWER 6 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-471376 [50] WPIDS
CR 2000-687101 [67]

DNC C2002-134015
TI Immunogenic composition useful for treating patients suffering from cancer comprising cancer antigens e.g., MAGE, prostase, along with **adjuvant** combination comprising immunostimulatory oligonucleotide and saponin.
DC B04 D16
IN GARCON, N; GERARD, C M G; STEPHENNE, J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 97
PI WO 2002032450 A2 20020425 (200250)* EN 49p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002044337 A 20020429 (200255)
ADT WO 2002032450 A2 WO 2001-EP11984 20011016; AU 2002044337 A AU 2002-44337 20011016
FDT AU 2002044337 A Based on WO 200232450
PRAI US 2000-690921 20001018; GB 2000-25573 20001018; GB 2000-25574 20001018
AB WO 200232450 A UPAB: 20030429
NOVELTY - New Immunogenic composition (I) comprises:
(a) a cancer **antigen** (CA) e.g. MAGE or prostase antigens linked to heterologous fusion partner, prostase fragments comprising at least 20 amino acids of prostase, mutated prostase, P501S, Cripto, or Her2-neu derivatives devoid of substantial portion of Her-2 neu transmembrane domain, and
(b) **adjuvant** comprising saponin and immunostimulatory oligonucleotide.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of a combination of a saponin and immunostimulatory oligonucleotide and a CA in the manufacture of a medicament for the treatment or prophylaxis of tumors.
ACTIVITY - Cytostatic; antimicrobial; antiallergic; immunosuppressive.
MECHANISM OF ACTION - Vaccine.
A range of **adjuvant** formulations with the **antigen** which was a fusion of the extracellular domain of Her 2 neu linked to the phosphorylation domain (ECD-PD) (ECD-PD with no **adjuvant** (group 1) and ECD-PD with **liposomes** with QS21 and with any of the **adjuvant** combinations 3D-MPL in membrane, tocol containing oil in water **emulsion** with QS21 and 3D-MPL CpG, **liposomes** with QS21 and 3D-MPL in membrane +CpG, tocol containing oil in water **emulsion** with QS21 and 3D-MPL+CpG, 3D-MPL+CpG, QS21+CpG, tocol containing oil in water **emulsion**+CpG, **liposomes** with QS21 in membrane+CpG, **liposomes** with 3D-MPL in membrane+CpG (groups 2-11, respectively)) which was produced in Chinese hamster ovary (CHO) cells according to the methods of WO 00/44899, was investigated. Groups of B6F1 mice were vaccinated on four occasions (in 50 mu l volumes), intramuscularly, 14 days apart. 14 days post the 4th vaccine dose, the mice were challenged subcutaneously with 2 x 106 TC1 tumor cell expressing the Her 2 neu. The Her 2 neu TC1 tumor cell lines was produced by transduction of TC1 cells by retroviral vectors coding for Her 2 neu. After a selection period with blastocydin, resistant clones were isolated and screened by fluorescence activated cell sorting (FACS) for Her 2 neu expression. The clone with the highest Her 2 neu expression was selected, and the challenge dose of 2 x 106 was identified to have a similar kinetic of growth as the wild-type TC1 cells and to give rise to a developing tumor in 100% of the control animals. The only vaccines that induced a complete regression of the tumor were vaccine containing both an immunostimulatory oligonucleotide and a saponin. The **adjuvant**

tested (AS1, AS2, AS7) had similar effect. However, the combination of AS1 and AS7 or AS2 and AS7 were more effective adjuvants. Cell-mediated immune response (CMI) was clearly shown after 4 vaccinations in animals receiving the combined **adjuvant** on the whole molecule ECD-PD, but also on each part separately (ECD and ICD). The formulations were very effective in inducing tumor regression.

USE - (I) is useful for treating a patient suffering from susceptible to a cancer expressing a Her 2 neu or prostate specific/tumor **antigen**. (I) is also useful for treating a patient suffering from or susceptible to a cancer expressing any of MAGE, prostase, P501S or Cripto (claimed).

The formulations containing tumor antigens are useful for immunotherapeutic treatment of prostate, breast, colorectal, lung, pancreatic, renal, or melanoma cancers. (I) is useful for inducing an immune response in an individual, and for treating a mammal susceptible to or suffering from an infectious disease or cancer, or allergy or autoimmune disease. (I) is useful as a medicament.

ADVANTAGE - The immunostimulatory oligonucleotides (CpG) and saponin and optionally a lipopolysaccharide combination are extremely potent adjuvants. The oligonucleotides in the **adjuvant** and vaccine compositions act synergistically with the combined saponin/lipopolysaccharide in the induction of **antigen** specific immune responses leading to enhanced tumor regression. The formulations are potent in the induction of immune responses conventionally associated with Th-1 type immune system. Her 2 neu antigens that are formulated with 3D-MPL, QS21 and CpG oligonucleotide together with **liposome** or oil-in-water **emulsion carrier**, produce both a humoral and cell mediated response in comparison to the formulations containing only CpG that do not produce a significant cell-mediated immune response.
Dwg.0/14

L17 ANSWER 7 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-454763 [48] WPIDS
DNC C2002-129354
TI Composition useful as vaccine comprises **carrier**, **liposome**, **antigen** and **adjuvant**.
DC B04 C03 D16
IN BROWN, R G; KIMMINS, W C; POHAJDAK, W
PA (BROW-I) BROWN R G;. (KIMM-I) KIMMINS W C; (POHA-I) POHAJDAK W; (IMMU-N) IMMUNOVACCINE TECHNOLOGIES INC
CYC 98
PI WO 2002038175 A1 20020516 (200248)* EN 66p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002110568 A1 20020815 (200256)
AU 2002014861 A 20020521 (200260)
ADT WO 2002038175 A1 WO 2001-CA1530 20011031; US 2002110568 A1 Provisional US 2000-246075P 20001107, Provisional US 2001-307159P 20010724, US 2001-992149 20011106; AU 2002014861 A AU 2002-14861 20011031
FDT AU 2002014861 A Based on WO 200238175
PRAI US 2001-307159P 20010724; US 2000-246075P 20001107; US 2001-992149 20011106
AB WO 200238175 A UPAB: 20020730
NOVELTY - A composition (I) comprises a **carrier** (C), **liposomes**, an **antigen** and an **adjuvant** (A). (C) comprises a continuous phase of hydrophobic substance.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the following:

(1) preparing (I) involving:

(a) encapsulating an **antigen** or an **antigen/adjuvant** complex in **liposomes** to form **liposome**-encapsulated **antigen**;

(b) mixing the **liposome**-encapsulated **antigen** with (C), and

(c) optionally adding (A) if **antigen/adjuvant** complex is not used in step (a).

USE - As a vaccine composition (claimed).

ADVANTAGE - The composition provides effective long-term immunocontraception in a mammal. The composition is free of lipid A. The composition potentiates and enhances an immune response in an animal. A single dose of the composition provides long-term immune response in a variety of species, typically not requiring boosters. The **antigen** used elicits an antibody that recognizes a native epitope in mammals such as horse, rabbit, deer and cat.

Dwg.0/1

L17 ANSWER 8 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-362308 [39] WPIDS
CR 2002-351845 [38]
DNC C2002-102545
TI Novel immunogenic composition comprising Streptococcus pneumoniae polysaccharide and protein **antigen** useful for preventing, ameliorating and treating pneumococcal infections in infants, toddlers and elderly persons.
DC B04 D16
IN LAFERRIERE, C A J; POOLMAN, J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA
CYC 98
PI WO 2002022167 A2 20020321 (200239)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002020548 A 20020326 (200251)
EP 1317279 A2 20030611 (200339) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002022167 A2 WO 2001-EP10568 20010912; AU 2002020548 A AU 2002-20548 20010912; EP 1317279 A2 EP 2001-984626 20010912, WO 2001-EP10568 20010912
FDT AU 2002020548 A Based on WO 200222167; EP 1317279 A2 Based on WO 200222167
PRAI GB 2000-22742 20000915
AB WO 200222167 A UPAB: 20030619

NOVELTY - An immunogenic composition (I) comprising at least one Streptococcus pneumoniae polysaccharide **antigen** and at least one S. pneumoniae protein **antigen** selected from PhtA, PhtD, PhtB, PhtE, SpsA, LytB, LytC, LytA, Sp125, Sp101, Sp128, Sp130 and Sp133, or its immunologically functional equivalent, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine (II) comprising (I); and

(2) making (I) involves selecting one or more pneumococcal polysaccharide **antigen**(s) and one or more pneumococcal protein **antigen**(s), and mixing the polysaccharide and protein antigens with a suitable excipient.

ACTIVITY - Auditory; antiinflammatory.

No biological data is given.

MECHANISM OF ACTION - Vaccine (claimed); inducer of T-cell mediated response against pneumococcal disease.

The impact of the addition of a Streptococcus pneumoniae protein plus

or minus 3D-MPL **adjuvant** on the protective effectiveness of protein D (PD)-conjugated 11-valent polysaccharide vaccine against pneumococcal lung colonization in OF1 mice intranasally challenged with serotype 2, 4 or 6B was tested. The prophylactic efficacy of a vaccine containing the 11-valent polysaccharide-protein D conjugate, a S. pneumoniae protein and AlPO4+3D-MPL adjuvants, was compared to the classical AlPO4 adsorbed 11-valent polysaccharide-protein D conjugate formulation. Groups of 12 female 4 week old OF1 mice were immunized subcutaneously, with formulations containing 50 mu g AlPO4, 0.1 mg PS/serotype of PD-conjugated 11-valent polysaccharide vaccine + 50 mu g AlPO4, or 0.1 mu g PS/serotype of PD-conjugated 11-valent polysaccharide vaccine + 10 mu g S. pneumoniae protein + 50 mu g AlPO4 + 5 mu g 3D-MPL. Challenge was done at day 21 as a significant protection was conferred by the 11-valent polysaccharide conjugate vaccine supplemented with the S. pneumoniae protein and adjuvanted with AlPO4+MPL. On the contrary, no significant protection was observed in animals immunized with the 11-valent polysaccharide conjugate/AlPO4 formulation. This result proved that the addition of the protein and 3D-MPL **adjuvant** enhanced the effectiveness of the 11-valent polysaccharide conjugate vaccine against pneumonia.

USE - (I) is useful as a medicament. (II) is useful for preventing or ameliorating S. pneumoniae infection in a patient over 55 years, or in the manufacture of a medicament for the prevention or treatment of pneumonia in a patient over 55 years. (I) or (II) is useful in the manufacture of a medicament for preventing, ameliorating or treating otitis media in infants or toddlers (claimed).

Dwg.0/0

L17 ANSWER 9 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-114486 [15] WPIDS
DNC C2002-035220
TI Product for modulating or stimulating immune response comprises lipids having glycerol backbone with at least one alkyl or acyl chain e.g. phospholipid.
DC B04 B05 C03
IN PORTER, W L
PA (PORT-I) PORTER W L
CYC 97
PI WO 2001095914 A1 20011220 (200215)* EN 59p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001064079 A 20011224 (200227)
EP 1289530 A1 20030312 (200320) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001095914 A1 WO 2001-GB2568 20010613; AU 2001064079 A AU 2001-64079 20010613; EP 1289530 A1 EP 2001-938401 20010613, WO 2001-GB2568 20010613
FDT AU 2001064079 A Based on WO 200195914; EP 1289530 A1 Based on WO 200195914
PRAI GB 2000-28239 20001120; GB 2000-14437 20000614; GB 2000-26667 20001101
AB WO 200195914 A UPAB: 20020306
NOVELTY - Product comprises lipids having a glycerol backbone carrying at least one alkyl or acyl chain. The lipid is a phospholipid, glycolipid or a neutral lipid with 10-22C atoms in the hydrocarbon chain.

ACTIVITY - Immunostimulant; Immunomodulator.

In a test, chickens (age 1-21 days) received food supplemented with a 2:1 methanol/chloroform extract of Bacillus subtilis, at the rate of the extract obtained from 100 mg Bacillus subtilis dried biomass per kg of feed. The extract was applied to a dusty and finely granular preparation

of expanded mica containing a high proportion of particles of 0.2-100 mu m before incorporating into the feed. The growth rate of treated chickens exceeded that of controls by 14.1%.

MECHANISM OF ACTION - None given in source material.

USE - Used for stimulating, modulating, promoting and/or modifying immune response in animals and humans, such as for suppressing rather than enhancing the immune response to antigenic stimulus e.g. in the control of immune diseases (all claimed). The product is used for enhancing or modulating the mucosal and systemic immune response to antigenic challenge for preventing and treating infectious and immune disease.

ADVANTAGE - The product facilitates access to the immune system to stimulate immunicity and/or to modulate the immune response to antigenic stimulus.

Dwg.0/15

L17 ANSWER 10 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-049090 [06] WPIDS
DNC C2002-013695
TI New non-peptide **antigen** from Mycobacterium tuberculosis, useful as a vaccine for eliciting or stimulating an immune against Mycobaterium tuberculosis, especially as a phophylactic or therapeutic treatment.
DC A96 B04 D16
IN BELTZ, G; COX, D; KENSIL, C; LECLAIR, K; LIU, G; BELTZ, J
PA (ANTI-N) ANTIGENICS INC; (BELT-I) BELTZ G; (COXD-I) COX D; (KENS-I) KENSIL C; (LECL-I) LECLAIR K; (LIUG-I) LIU G; (AQUI-N) AQUILA BIOPHARMACEUTICALS INC
CYC 95
PI WO 2001075096 A1 20011011 (200206)* EN 57p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001051316 A 20011015 (200209)
US 2002044951 A1 20020418 (200228)
ADT WO 2001075096 A1 WO 2001-US11016 20010404; AU 2001051316 A AU 2001-51316 20010404; US 2002044951 A1 Provisional US 2000-194519P 20000404, US 2001-825789 20010404
FDT AU 2001051316 A Based on WO 200175096
PRAI US 2000-194519P 20000404; US 2001-825789 20010404
AB WO 200175096 A UPAB: 20020128

NOVELTY - A non-peptide **antigen** (I) isolated and purified from Mycobacterium tuberculosis, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of enhancing an immune response in a mammal to Mycobacterium tuberculosis by administering a vaccine composition comprising (I);

(2) a vaccine composition comprising (I), where the vaccine enhances an immune response to M. tuberculosis in a mammal to which the vaccine is administered;

(3) a pharmaceutical composition comprising (I) and a vehicle;

(4) a vaccine composition comprising one or more non-peptide **antigen** isolated and purified from M. tuberculosis and at least one lipid **carrier**, where the vaccine comprises vesicles; and

(5) a method of making a vaccine composition comprising extruding a mixture of one or more lipid carriers, and one or more isolated non-peptide antigens through a filter membrane.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

USE - (I) is useful as vaccine component for stimulating or eliciting an immune response against Mycobacterium tuberculosis, especially as a

therapeutic or prophylactic treatment.
Dwg.0/13

L17 ANSWER 11 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-476107 [51] WPIDS
DNC C2001-142806
TI New pharmaceutical compositions, useful as vaccines for treating or preventing neurodegenerative disorders, e.g. Alzheimer's Disease, loss of cognitive function, senile dementia, Parkinson's disease or cerebral palsy.
DC B04 D16
IN SRIVASTAVA, P K
PA (UYCO-N) UNIV CONNECTICUT HEALTH CENT
CYC 22
PI WO 2001053457 A2 20010726 (200151)* EN 47p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU CA JP
AU 2001029592 A 20010731 (200171)
ADT WO 2001053457 A2 WO 2001-US1665 20010118; AU 2001029592 A AU 2001-29592 20010118
FDT AU 2001029592 A Based on WO 200153457
PRAI US 2000-489219 20000121
AB WO 200153457 A UPAB: 20010910
NOVELTY - A pharmaceutical composition, which comprises a pharmaceutical **carrier** and an immunogenic amount of an antigenic molecule for treating or preventing a neurodegenerative disorder, is new. The antigenic molecule displays the antigenicity of an **antigen** associated with a neurodegenerative disorder, with the proviso that the antigenic molecule is not beta amyloid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) recombinant cells transformed with:

(a) a nucleic acid comprising a sequence that is operably linked to a promoter, where the nucleic acid encodes a fusion protein that has an antigenic molecule operatively linked to a **carrier** protein, and where antigenic molecule displays the antigenicity of an **antigen** associated with a neurodegenerative disorder; or

(b) nucleic acid comprising either:

(i) a first nucleic acid having a first nucleotide sequence that is operably linked to a first promoter and encodes an antigenicity of an **antigen** associated with a neurodegenerative disorder, and

(ii) a second nucleic acid comprising a second nucleic acid sequence that is operably linked to a second promoter and encodes a **carrier** protein, such that the antigenic molecule and the **carrier** protein are expressed within the cell and non-covalently associate with each other to form a complex that in sufficient amount is capable of eliciting an immune response to the antigenic molecule;

(2) a method for preparing a fusion protein capable of eliciting an immune response against a neurodegenerative disorder comprising:

(a) culturing the recombinant cell; and

(b) recovering the fusion protein from the cells;

(3) a method of mixing the **carrier** with one or more antigenic molecules in vitro, where one or more antigenic molecules display the antigenicities of antigens associated with a neurodegenerative disorder, comprising:

(a) incubating the antigenic molecule or molecules with a **carrier** protein for formation of the complex; and

(b) isolating the complexes;

(4) a method for eliciting an immune response against an **antigen** associated with a neurodegenerative disorder in an individual by administering to the individual the antigenic molecule that displays the antigenicity of an **antigen** associated with a neurodegenerative disorder; and

(5) methods of treating or protecting against a neurodegenerative disorder in an individual having a neurodegenerative disorder, or in whom prevention of a neurodegenerative disorder is desired, comprising administering to the individual the composition or the fusion protein cited above.

ACTIVITY - Neuroprotective; nootropic; neuroleptic; cerebroprotective; antiparkinsonian; anticonvulsant.

No details of clinical tests are given.

MECHANISM OF ACTION - Vaccine.

USE - The pharmaceutical composition is useful for treating or preventing neurodegenerative disorders. The neurodegenerative disorders include Alzheimer's Disease, age-related loss of cognitive function, senile dementia, Parkinson's disease, amyotrophic lateral sclerosis, Wilson's Disease, cerebral palsy, progressive supranuclear palsy, Guam disease, Lewy body dementia, prion diseases, spongiform encephalopathies, Creutzfeldt-Jakob disease, polyglutamine diseases, Huntington's disease, myotonic dystrophy, Freidrich's ataxia, Gilles de la Tourette's syndrome, seizure disorders, epilepsy, chronic seizure disorder, stroke, brain trauma, spinal cord trauma, AIDS dementia, alcoholism, autism, retinal ischemia, glaucoma, autonomic function disorder, hypertension, neuropsychiatric disorder, schizophrenia or schizoaffective disorder (all claimed). The pharmaceutical composition is particularly useful as vaccines for treating or preventing the diseases cited above.

Dwg.0/0

L17 ANSWER 12 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-398076 [42] WPIDS
DNC C2001-121056
TI Novel vaccine composition useful for treatment or prophylaxis of toxoplasmosis infections, comprises toxoplasma protein, SAG3, its immunogenic derivative, or a truncated toxoplasma protein.
DC B04 D16
IN BIEMANS, R; BOLLEN, A; DE NEVE, J; HAUMONT, M; JACQUET, A
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 94
PI WO 2001043768 A2 20010621 (200142)* EN 45p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001031588 A 20010625 (200162)
ADT WO 2001043768 A2 WO 2000-EP12704 20001212; AU 2001031588 A AU 2001-31588 20001212
FDT AU 2001031588 A Based on WO 200143768
PRAI GB 1999-29434 19991213
AB WO 200143768 A UPAB: 20010726
NOVELTY - A vaccine composition (I) comprising toxoplasma protein, SAG3 with a sequence (S) comprising 385 amino acids fully defined in the specification, or its immunogenic derivative, or comprising a truncated toxoplasma protein which comprises amino acid residues 40-359 of (S) or its immunogenic derivative, in combination with a suitable **adjuvant** and/or **carrier**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a SAG3 protein (II) of a sequence (S), or its immunogenic derivative; and

(2) a DNA sequence (III) comprising 1446 base pairs fully defined in the specification, encoding (II).

ACTIVITY - Protozoacide.

Guinea pigs were immunized with recombinant SAG3 formulated with an **adjuvant** comprising 3D-MPL and a non-reactogenic form of QS21, or

the **adjuvant** alone. After immunization, animals were bled and sera were tested for the presence of anti-SAG3 IgG antibodies. Before **antigen** injection, all guinea pigs were monitored for absence of seroreactivity against Toxoplasma. Females were mated with males for breeding after immunization, and infected using 5.105 tachyzoites. Infectious status of pups delivered from guinea pigs was evaluated in a mouse assay, pups were sacrificed within 48 hours following delivery, each brain was homogenized in phosphate buffered saline (PBS) and injected into two female BalbC mice. Mice that did not survive from 21 days onwards after brain homogenate injection were considered infected and their mortality indicated the infection status of the pups. In was assessed that a pup was infected once one of the two injected mice died. After challenge, 15 SAG3 and 16 mock-immunized guinea pigs produced respectively 52 and 58 pups of which 4 and 20 respectively were excluded for further analysis because, as stillborn pups or pups retrieved from dead mother were always negative in the mouse assay even if they originated from the mock-immunized group, probably due to parasite inactivation. After exclusion, 48 and 38 pups, originated from 15 and 11 litters respectively, were analyzed. Protection against vertical transmission was observed. The results showed that the proportion of infected pups were less in SAG3 immunized group when compared to the mock-immunized group.

MECHANISM OF ACTION - Vaccine (claimed).

USE - (I) is useful in medical therapy, for treatment or prophylaxis of toxoplasmosis infections. (I) is useful in the prevention of both horizontal and vertical (congenital) transmission of toxoplasmosis.

Dwg.0/10

L17 ANSWER 13 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-594516 [56] WPIDS
CR 2000-594515 [56]; 2000-594517 [56]; 2000-679550 [66]; 2001-006956 [01]
DNC C2000-177616
TI Novel immunogenic composition comprising at least 1 polysaccharide **antigen** and at least 1 protein **antigen** from Streptococcus pneumoniae, useful in vaccines for treating pneumonia and otitis media.
DC B04 D16
IN CAPIAU, C; DESCHAMPS, M; DESMONS, P M; LAFERRIERE, C A J; POOLMAN, J; PRIEELS, J; FERRIERE, C A J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 92
PI WO 2000056359 A2 20000928 (200056)* EN 77p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000038136 A 20001009 (200103)
BR 2000009166 A 20011226 (200206)
EP 1162999 A2 20011219 (200206) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CZ 2001003379 A3 20020313 (200223)
KR 2002001785 A 20020109 (200246)
HU 2002000373 B 20020628 (200255)
AU 750762 B 20020725 (200260)
ZA 2001007638 A 20020828 (200264) 97p
JP 2002540074 W 20021126 (200307) 97p
CN 1391481 A 20030115 (200330)
ADT WO 2000056359 A2 WO 2000-EP2467 20000317; AU 2000038136 A AU 2000-38136 20000317; BR 2000009166 A BR 2000-9166 20000317, WO 2000-EP2467 20000317; EP 1162999 A2 EP 2000-916983 20000317, WO 2000-EP2467 20000317; CZ 2001003379 A3 WO 2000-EP2467 20000317, CZ 2001-3379 20000317; KR

2002001785 A WO 2000-EP2467 20000317, KR 2001-711941 20010919; HU 2002000373 B WO 2000-EP2467 20000317, HU 2002-373 20000317; AU 750762 B AU 2000-38136 20000317; ZA 2001007638 A ZA 2001-7638 20010917; JP 2002540074 W JP 2000-606263 20000317, WO 2000-EP2467 20000317; CN 1391481 A CN 2000-807773 20000317

FDT AU 2000038136 A Based on WO 200056359; BR 2000009166 A Based on WO 200056359; EP 1162999 A2 Based on WO 200056359; CZ 2001003379 A3 Based on WO 200056359; KR 2002001785 A Based on WO 200056359; HU 2002000373 B Based on WO 200056359; AU 750762 B Previous Publ. AU 200038136, Based on WO 200056359; JP 2002540074 W Based on WO 200056359

PRAI GB 1999-16677 19990715; GB 1999-6437 19990319; GB 1999-9077 19990420; GB 1999-9466 19990423

AB WO 200056359 A UPAB: 20030513

NOVELTY - Immunogenic composition (I) comprising at least 1 Streptococcus pneumoniae polysaccharide **antigen** and at least 1 S. pneumoniae protein **antigen** or immunologically functional equivalent, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of making an immunogenic composition comprising:

(1) selecting at least 1 pneumococcal polysaccharide **antigen**;

(2) selecting at least 1 pneumococcal protein **antigen**; and

(3) mixing the polysaccharide and protein antigens with a suitable excipient.

ACTIVITY - Antibacterial; antiinflammatory; auditory.

MECHANISM OF ACTION - Vaccine.

Balb/c mice (1 year old) were immunized with 1/10th of the human dose of a pneumococcal-polysaccharide/ protein D conjugate vaccine, or 23-valent plain polysaccharide vaccine. Groups of 20 mice were immunized intramuscularly on days 0 and 21 and test bleeds were obtained on day 35. The sera were enzyme-linked immunosorbant antibody (ELISA) tested for IgG antibodies to the pneumococcal polysaccharides. The results showed that immunization with plain polysaccharides did not produce significant amounts of IgG antibodies. Immunization with conjugate vaccines induced IgG antibody with high seroconversion rates against all serotypes except 23F and 2 doses of vaccine formulated with 3D-MPL induced the highest GMC specific IgG and this was statistically significant for all serotypes except 23F, in which case it had a significantly higher seroconversion rate.

USE - (I) is useful as a vaccine, especially (with a TH1 inducing **adjuvant**) for preventing or ameliorating S. pneumoniae infection and pneumonia in a patient over 55 years, and/or preventing or ameliorating otitis media in infants (claimed).

Dwg.0/1

L17 ANSWER 14 OF 18 WPIDS (C) 2003 THOMSON DERWENT

AN 2000-106101 [09] WPIDS

DNN N2000-081471 DNC C2000-031931

TI Method for production of toxoplasma **antigen** SAG1 for use in vaccines.

DC B04 D16 S03

IN BIEMANS, R; BOLLEN, A; HAUMONT, M

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS

CYC 87

PI WO 9966043 A1 19991223 (200009)* EN 47p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

AU 9945102 A 20000105 (200024)

EP 1086228 A1 20010328 (200118) EN

R: BE CH DE ES FR GB IT LI NL
ADT WO 9966043 A1 WO 1999-EP3957 19990608; AU 9945102 A AU 1999-45102 19990608; EP 1086228 A1 EP 1999-927922 19990608, WO 1999-EP3957 19990608
FDT AU 9945102 A Based on WO 9966043; EP 1086228 A1 Based on WO 9966043
PRAI GB 1999-8564 19990415; GB 1998-12773 19980612
AB WO 9966043 A UPAB: 20000218
NOVELTY - A novel method for the production of the toxoplasma **antigen** SAG1 or a fragment of it, comprises constructing a plasmid comprising DNA encoding SAG1 or a fragment of it, transforming a P. pastoris host cell with the plasmid, and culturing the host cell such that the DNA encoding SAG1 or a fragment of it is expressed.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) the plasmid pNIV3488;

(2) a SAG1 protein or fragment expressed in P. pastoris;

(3) a vaccine composition comprising the protein of (2) in combination with a suitable **adjuvant** and/or **carrier**;

(4) a truncated SAG1 protein in which the anchor region of SAG1 is absent;

(5) a vaccine composition comprising the protein of (4) in combination with a suitable **adjuvant** and/or **carrier**;

(6) use of the protein of (2) or (4) in the manufacture of a medicament for the prevention or treatment of toxoplasmosis infections in mammals; and

(7) a diagnostic kit for the diagnosis of toxoplasmosis infection in the blood of mammals which may be infected, the kit comprises an anchor-less SAG1 **antigen** or a fragment of it.

ACTIVITY - Protozoacide.

MECHANISM OF ACTION - Vaccine.

USE - The SAG1 protein, fragment, and truncated variant can be used in the manufacture of a medicament for the prevention or treatment of toxoplasmosis in mammals (claimed).

ADVANTAGE - None given.

Dwg.0/0

L17 ANSWER 15 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-072546 [06] WPIDS
DNC C2000-020733
TI New polypeptides, useful to produce vaccines for neosporosis in animals, especially livestock.
DC B04 C06 D16
IN ATKINSON, R; ELLIS, J T; RYCE, C
PA (INSE-N) INSEARCH LTD
CYC 25
PI WO 9961046 A1 19991202 (200006)* EN 60p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA NO NZ US
AU 9941229 A 19991213 (200020)
EP 1085898 A1 20010328 (200118) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
AU 735498 B 20010712 (200147)
ADT WO 9961046 A1 WO 1999-AU405 19990526; AU 9941229 A AU 1999-41229 19990526; EP 1085898 A1 EP 1999-924579 19990526, WO 1999-AU405 19990526; AU 735498 B AU 1999-41229 19990526
FDT AU 9941229 A Based on WO 9961046; EP 1085898 A1 Based on WO 9961046; AU 735498 B Previous Publ. AU 9941229, Based on WO 9961046
PRAI AU 1998-3717 19980526
AB WO 9961046 A UPAB: 20000203
NOVELTY - An isolated polypeptide (I) forming a Neospora caninum **antigen** is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) An isolated nucleic acid molecule (II) encoding (I) comprising:

(a) a 636 (A) or a 1712 bp (B) sequence as given in the

specification;
(b) functional equivalents or portions of (A) or (B);
(c) sequences which hybridize to (A) or (B); or
(d) sequences which have at least 60% homology with (A) or (B).
(2) A vector (III) comprising (II);
(3) A composition (IV) comprising (I), mixtures of or immunogenic fragments of (I); and
(4) A composition (V) comprising (III) and a **carrier**.
ACTIVITY - Anti-protozoal.
MECHANISM OF ACTION - Vaccine.
USE - The polypeptides and vectors are useful in obtaining a protective effect against neosporosis in animals (claimed). (IV) (especially comprising sequence D) and (V) (especially when the plasmid is VR1012 and includes sequence A or B) can be used to raise an immune response against neosporosis in animals (claimed), i.e. in vaccines to protect animals against neosporosis. The polypeptides (especially NcGra2) are also useful to detect antibodies reactive or specific to Neospora (claimed) e.g. to screen herds for infected animals or to determine the effectiveness of immunization. The polypeptides may be used to produce antibodies, also useful in assays to detect N. caninum to protect against neosporosis.
ADVANTAGE - The polypeptides allow for development of vaccines for neosporosis, which may be practical for controlling the disease in cattle, unlike current chemical treatment.
Dwg.0/8

L17 ANSWER 16 OF 18 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-620288 [53] WPIDS
DNC C1999-181049
TI Enhancing mammalian immune response, useful for treating individuals suffering from an immuno-compromised disease or disorder e.g. AIDS and/or for use with chemotherapy recipients.
DC B04 D16
IN BRENNER, M B; DASCHER, C C; HIROMATSU, K; PORCELLI, S A
PA (BGHM) BRIGHAM & WOMENS HOSPITAL INC; (BGHM) BRIGHAM WOMENS HOSPITAL INC
CYC 86
PI WO 9952547 A1 19991021 (199953)* EN 49p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9935588 A 19991101 (200013)
EP 1071452 A1 20010131 (200108) EN
R: AT BE DE ES FI FR GB IE IT SE
JP 2002511421 W 20020416 (200242) 52p
ADT WO 9952547 A1 WO 1999-US8112 19990413; AU 9935588 A AU 1999-35588 19990413; EP 1071452 A1 EP 1999-917473 19990413, WO 1999-US8112 19990413; JP 2002511421 W WO 1999-US8112 19990413, JP 2000-543157 19990413
FDT AU 9935588 A Based on WO 9952547; EP 1071452 A1 Based on WO 9952547; JP 2002511421 W Based on WO 9952547
PRAI US 1998-81638P 19980413
AB WO 9952547 A UPAB: 20011203
NOVELTY - A method of enhancing an immune response in a mammal to at least one CD1 **antigen** is new and comprises co-administering to the mammal an effective amount of at least one CD1 **antigen** and at least one T cell stimulating compound.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method of vaccinating a mammal against at least one CD1 **antigen** comprising administering to the mammal an effective amount of at least one CD1 **antigen** and at least one **adjuvant**;

(2) a method of stimulating a CD1-restricted immune response in a mammal comprising administering to the mammal a composition comprising at least one **adjuvant** and at least one lipid **antigen** where the **antigen** elicits a CD1-restricted immune response;

(3) an immunogenic composition (I), comprising:

(a) at least one T cell stimulating compound; and

(b) at least one CD1 **antigen**, where the CD1 **antigen** elicits a CD1-restricted immune response;

(4) a method for eliciting an immunogenic response in a mammal comprising administering (I);

(5) a vaccine composition (II) comprising at least one **adjuvant** and at least one lipid **antigen** where the lipid **antigen** elicits a CD1-restricted immune response;

(6) a method for vaccinating a mammal comprising administering (II); and

(7) a kit comprising at least one T-cell stimulating compound and at least one CD1 **antigen** where the CD1 **antigen** elicits a CD1-restricted immune response.

ACTIVITY - Anti-parasitic; antibacterial; immune stimulant.

MECHANISM OF ACTION - The method elicits at least one immunological parameter e.g. antibody response the **antigen**, cytotoxic T-lymphocyte response, T-cell proliferation, helper T-cell response or a T-cell modulated cytokine response.

USE - The method is useful for enhancing or boosting the immune response of an individual who has a immuno-compromised disease, disorder or condition (e.g. AIDS or chemotherapy recipient). The method is also useful for eliciting or boosting an immune response for at least one bacterial infection (e.g. Mycobacteria genus, Hemophilus genus, Streptococcus genus, Staphylococcus genus and Chlamydia) and/or at least one parasitic infection (e.g. Plasmodium or Trypanosoma genus). (All claimed). The CD1 **antigen** can also be a tumor associated or derived **antigen** that is involved in diseases e.g. cancer (e.g. melanoma, breast cancer, prostate cancer, and colo-rectal cancer) or a self **antigen** that is involved in autoimmune diseases (e.g. diabetes, Lupus, rheumatoid arthritis).

ADVANTAGE - The method enhances the immune response for vaccines without eliciting a sufficient protective immune response in a host.

Dwg.0/7

L17 ANSWER 17 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI

AN 2003-07170 BIOTECHDS

TI Recovering immunogenic outer membrane associated polypeptides from microbial cells, useful for inducing passive or active immunization against bacterial, fungal or protozoan infection, comprises culturing cells in iron-starved conditions;
recombinant protein production and antibody for use in disease therapy

AU SCOTT D L; THOMAS C B; SMALLS F; WILLIAMS M

PA D-SQUARED BIOTECHNOLOGIES INC

PI WO 2002083843 24 Oct 2002

AI WO 2002-US11110 10 Apr 2002

PRAI US 2001-304390 10 Jul 2001; US 2001-282809 10 Apr 2001

DT Patent

LA English

OS WPI: 2003-067575 [06]

AB DERWENT ABSTRACT:

NOVELTY - Recovering immunogenic outer membrane associated polypeptides (OMAPs) from microbial cells comprises: (a) culturing microbial cells or bacterial cells in iron-starved conditions to up-regulate OMAPs; (b) harvesting membranes from cells, and solubilizing (bacterial) membrane proteins; (c) purifying OMAPs from contaminating immunosuppressive endotoxins; and (d) purifying OMAPs from their binding ligands.

DETAILED DESCRIPTION - Recovering immunogenic outer membrane associated polypeptides (OMAPs) from microbial cells comprises: (a)

culturing microbial cells or bacterial cells in iron-starved conditions to up-regulate OMAPs; (b) harvesting membranes from cells, and solubilizing (bacterial) membrane proteins; (c) purifying OMAPs from contaminating immunosuppressive endotoxins; and (d) purifying OMAPs from their binding ligands. The purified OMAPs from the microbial cells are substantially endotoxin-free and ligand-free, and are capable of generating an OMAP specific immunoresponse when injected into a host. The OMAPs comprise the Scott-Thomas domain and the D2 domain, where the D2 domain is selected from the group of D2 domain 1, D2 domain 3, or D2 domain 4. INDEPENDENT CLAIMS are also included for the following: (1) Isolated nucleotide sequence that encodes an epitope of FptA that contains a siderophore binding site; (2) Producing (M1) anti-OMAPs antibody; (3) Vaccine for immunizing an animal against microbial infection comprising a non-iron-regulated OMAP recovered by M1, and a physiologic **carrier**; (4) Immunizing (M2) an animal against a bacterial infection; (5) Diagnostic kits for detecting OMAPs in a biological sample comprising: (a) primer pair for amplifying a nucleic acid, where the oligonucleotide primers are at least 14 bases in length; or (b) oligonucleotide probe that binds under high stringency conditions to the isolated nucleic acid cited above; and (c) containers for each of the primers, or for the probe; (6) Recovering (M3) OMAPs from fungi, gram-negative bacteria and gram-positive bacteria species; (7) Actively immunizing (M4) a host animal or human using OMAPs of (6) for the recovery of surface exposed immunogenic polypeptides from gram-negative bacteria and gram-positive bacteria species; (8) Inducing (M5) passive immunization of a host, where one or more surface exposed immunogenic fragments comprising any one of 15 sequences consisting of 19-350 amino acids fully defined in the specification, generate specific antibodies in an animal or human and provide prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species; and (9) Preventing (M6) or treating wound infections or sepsis caused by gram-negative and gram-positive bacteria species.

BIOTECHNOLOGY - Preferred Methods: Recovering immunogenic OMAPs from microbial cells comprises: (a) culturing the microbial cells in iron-starved condition to up-regulate OMAPs, where the OMAPs are preferably comprised of D2 domain 4; (b) purifying OMAPs from contaminating immunosuppressive endotoxins; and (c) further purifying OMAPs from their binding ligands. The D2 domains 1, 3 and 4 comprise a fully defined sequence of 97, 428 and 82 amino acids, respectively, given in the specification. Particularly, recovering immunogenic OMAPs from Stenotrophomonas maltophilia strain comprises: (a) culturing the S. maltophilia strain in iron-starved conditions to up-regulate OMAPs; (b) harvesting membrane from S. maltophilia, and solubilizing the membrane proteins; (c) purifying OMAPs from contaminating immunosuppressive endotoxins; and (d) further purifying OMAPs from their binding ligands; where the purified OMAPs from S. maltophilia are substantially endotoxin-free and ligand-free, and are capable of generating an OMAP specific immunoresponse when injected into a host. Recovering OMAPs from fungi, gram-negative bacteria and gram-positive bacteria species comprises: (a) propagation of fungi, gram-negative bacteria and gram-positive bacteria species in condition of low iron; (b) separation of membrane associated polypeptides, including receptors for iron-binding molecules (i.e. siderophore receptors) that are complexed with there iron-binding ligands, from other components of the cell wall of either gram-negative and gram-positive bacteria species; and (c) separation of siderophore receptors from their iron-binding ligands. M1 comprises: (a) culturing from bacteria, fungi, or protozoans cells, e.g. S. maltophilia cells, in iron-starved condition to up-regulate OMAPs; (b) purifying OMAPs from contaminating immunosuppressive endotoxins and ligands; (c) generating antisera by using purified OMAPs to animals; (d) purifying anti-OMAPs immunogobulins; and (e) characterizing the anti-OMAPs. M1 further comprises producing anti-OMAP Fab fragments by separating IgG molecules into Fab and Fc fragments. M2 comprises administering the

vaccine of (3). The vaccine induces an immunologically effective antibody titer in the host to prevent or eliminate the infection without administration of a booster of the vaccine. M4 comprises actively immunizing a vertebrate animal with gram negative and gram positive bacteria species comprising actively immunizing a vertebrate animal with gram-negative and gram-positive species membrane associated polypeptides, where the amount of the membrane associated polypeptides in a **carrier** is about 25-5000 microg/ml. M4 comprises: (a) isolating and purifying gram-negative and gram-positive bacteria species genomic DNA which is cloned into an appropriate vector and used to produced a cDNA expression library; (b) isolating and purifying gram-negative and gram-positive bacteria species membrane associated polypeptides antisera is used to probe expression library for surface exposed immunogenic polypeptides; (c) isolating and characterizing gram-negative and gram-positive bacteria species surface exposed immunogenic polypeptides; (d) identifying the surface exposed immunogenic polypeptides which possess sequence motifs comprising the sequences of 97, 428, and 82 amino acids fully defined in the specification; and (e) classifying and identifying epitopes in receptors of iron-binding ligands that are conserved amongst gram-negative, gram-positive and gram-negativegram-positive bacteria species comprising 15 sequences consisting of 19-350 amino acids fully defined in the specification. The polypeptide or the immunogenic fragment produces an antibody response in an animal or human singly or in combination for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. The **carrier**, which is a physiologic **carrier**, is a liquid, and the amount of the surface exposed immunogenic polypeptide(s) in the vaccine is about 25-5000 microg/ml. M5 comprises: (a) immunizing laying hens with immunogenic polypeptides or immunogenic fragments comprising any one of 15 sequences consisting of 19-350 amino acids fully defined in the specification; (b) recovering the anti- bacterial polyclonal antibodies from the egg yolks; and (c) purifying the polyclonal antibodies. The method uses one or more anti-bacterial monoclonal antibodies for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. Transgenic mice capable of producing high affinity human anti-bacterial mononclonal antibodies are also immunized using the method above. The method uses one or more anti-bacterial single-chain Fv (scFv) monoclonal antibodies for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. M5 comprises: (a) immunoglobulin genes from anti-bacterial monoclonal cell lines are cloned into an appropriate expression vector to produce scFv; (b) the anti-bacterial scFv monoclonal antibodies are generated; and (c) the monoclonal antibodies are administered for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. The anti-bacterial scFv monoclonal antibodies are also administered for neutralization of gram-negative and gram-positive bacteria species in a **carrier**. Preventing or treating wound infections or sepsis caused by gram-negative and gram-positive bacteria species by administering to an animal or human, the anti-bacterial polyclonal antibodies of (8) for the effective neutralization of gram-negative and gram-positive bacteria species in a **carrier**.

Preferred Vaccine: The vaccine stimulates the production of antibody to the OMAPs in an adult animal. The vaccine induces an immunologically effective antibody titre in the host to prevent or eliminate the infection without administration of a booster of the vaccine. The **carrier** is physiological saline, phosphate-buffered saline, Tris (hydroxymethyl aminomethane), or Tris-buffered saline. The **carrier** is in the form of a solution, water-in-oil **emulsion**, **liposomes**, or a metabolizable solid matrix. The vaccine further comprises an **adjuvant** selected from the group of aluminum hydroxide, aluminum phosphate, or Freund's Incomplete **Adjuvant**. Preferred Cells: The microbial cells are selected from

the group of bacteria, fungi, or protozoans, such as S. maltophilia, Bacillus cepcia, Cryptococcis neoformans, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus or Staphylococcus epidermidis. The microbial cells or bacteria can also be gram-negative bacteria, gram-positive bacteria, or mycobacteria.

ACTIVITY - Antibacterial; Fungicide; Protozoacide; Immunostimulant. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The methods are useful for recovering immunogenic OMAPs for inducing passive or active immunization against bacterial, fungal or protozoan infections. The antibodies are useful for diagnosing, preventing and treating bacterial, fungal or protozoan infections (claimed).

ADMINISTRATION - Loading dose is about 2.5 mg/kg. The vaccine is administrated by subcutaneous injection, intramuscular injection, sustained release repository, aerosolization, or inoculation into an egg (all claimed). Administration of the antibodies may be intravenous, subcutaneous, intramuscular, intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation.

EXAMPLE - An overnight culture of Stenotrophomonas maltophilia strain, designated D2-DLS01 was used to inoculate 500 ml of freshly prepared M9-minimal medium supplemented with maltose (10 g/ml), methionine (40 microg/ml), 1 M MgSO4 (0.1%), and the iron chelator 2'2' dipyridyl (100 microM). The cells were concentrated by centrifuging the culture. The concentrated bacteria were resuspended in 17 ml of HE buffer in a 50 ml sterile tube, then frozen in liquid nitrogen and thawed at room temperature. This step was repeated until the solution became viscous. Ten milliliters of the viscous lysate was layered to differentiate the cytoplasmic and membrane fractions and analyzed for iron reactive material and the presence of lipopolysaccharide (LPS). The iron reactivity and the LPS contamination were localized to the membrane fraction. The membrane fraction was resuspended in 50 ml of solubilization buffer and incubated for 1 hour at 4degreesC. The solubilized membranes were mixed with 10% polyethyleneimine (PEI). The iron reactivity was identified in the PEI supernatant while the LPS contamination molecules were localized to the PEI pellet. The iron reactive PEI supernatant (50 ml) was mixed by slow stirring with 18.05 g of ammonium sulfate and incubated with continuous stirring at 4degreesC for 1 hour. The iron-reactive fraction was recovered in the ammonium sulfate pellet, no LPS was detectable. The ammonium sulfate precipitate was resuspended in 25 ml of HE buffer and size fractionated by tangential-flow ultra centrifugation. The filtrate and retainate were analyzed for iron reactivity using the CAS assay and for the presence of LPS. The iron reactivity was found in the retainate, no LPS were detected in either fraction. The iron reactivity was transferred to the filtrate by the addition of solid urea to a final concentration of 6 M. The retainate, for D2-DLS01 **antigen** cocktail, was modified with 0.02% sodium azide and stored at -20degreesC. (91 pages)

L17 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2003 ACS
AN 2000:608610 CAPLUS
DN 133:206755
TI Immunogens comprising a peptide and a **carrier** derived from Haemophilius influenzae protein D
IN Coste, Michel; Lobet, Yves; Van-Mechelen, Marcelle Paulette; Verriest, Christophe
PA Smithkline Beecham Biologicals S.A., Belg.
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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PI   WO 2000050077      A1   20000831        WO 2000-EP1457   20000222
        W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
            CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
            IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
            MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
            SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
            DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
            CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1156825         A2   20011128        EP 2000-909235   20000222
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
     JP 2002537354      T2   20021105        JP 2000-600687   20000222
PRAI GB 1999-4405       A    19990225
     GB 1999-4408       A    19990225
     GB 1999-4412       A    19990225
     GB 1999-19260      A    19990813
     WO 2000-EP1457     W    20000222
AB   The present invention provides peptide immunogens linked to a
     carrier wherein the carrier is derived from Haemophilius
     Influenzae Protein D or fragments thereof.  Compns comprising the
     antigen peptide, protein D epitope or mimotope, and immune
     adjuvant (e.g. saponin, aluminum salt, oil in water
     emulsion, or liposome) are useful for treating infection
     or chronic diseases.
RE.CNT  6      THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 10:30:28 ON 24 JUN 2003)

     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS' ENTERED AT 10:30:55 ON 24 JUN 2003
                 E BROWN ROBERT GEORGE/AU
L1             6 S E3
                 E BROWN R G/AU
L2           972 S E3
                 E POHAJDAK BILL/AU
L3           211 S E2-E5
                 E KIMMINS WARWICK CHARLES/AU
L4            14 S E1-E3
                 E KIMMINS W C/AU
L5           115 S E2-E6
L6          1222 S L1-L5
L7             9 S L6 AND ADJUVANT
L8             5 DUP REM L7 (4 DUPLICATES REMOVED)
L9             7 S L7 AND LIPOSOM?
L10            4 DUP REM L9 (3 DUPLICATES REMOVED)
L11            2 S LIPOSOM? (5A) EMULSION (5A) ANTIGEN (5A) ADJUVANT
L12         8577 S LIPOSOM? AND ANTIGEN
L13         1436 S L12 AND ADJUVANT
L14            0 S L13 AND EMUSLION (10A) CARRIER
L15           96 S L13 AND EMULSION
L16           61 DUP REM L15 (35 DUPLICATES REMOVED)
L17           18 S L16 AND CARRIER

=> s l16 and continuous phase
L18            1 L16 AND CONTINUOUS PHASE
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=> d bib ab

L18 ANSWER 1 OF 1 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-454763 [48] WPIDS
DNC C2002-129354
TI Composition useful as vaccine comprises carrier, **liposome**, **antigen** and **adjuvant**.
DC B04 C03 D16
IN BROWN, R G; KIMMINS, W C; POHAJDAK, W
PA (BROW-I) BROWN R G; (KIMM-I) KIMMINS W C; (POHA-I) POHAJDAK W; (IMMU-N) IMMUNOVACCINE TECHNOLOGIES INC
CYC 98
PI WO 2002038175 A1 20020516 (200248)* EN 66p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002110568 A1 20020815 (200256)
AU 2002014861 A 20020521 (200260)
ADT WO 2002038175 A1 WO 2001-CA1530 20011031; US 2002110568 A1 Provisional US 2000-246075P 20001107, Provisional US 2001-307159P 20010724, US 2001-992149 20011106; AU 2002014861 A AU 2002-14861 20011031
FDT AU 2002014861 A Based on WO 200238175
PRAI US 2001-307159P 20010724; US 2000-246075P 20001107; US 2001-992149 20011106
AB WO 200238175 A UPAB: 20020730
NOVELTY - A composition (I) comprises a carrier (C), **liposomes**, an **antigen** and an **adjuvant** (A). (C) comprises a **continuous phase** of hydrophobic substance.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the following:
(1) preparing (I) involving:
(a) encapsulating an **antigen** or an **antigen/adjuvant** complex in **liposomes** to form **liposome**-encapsulated **antigen**;
(b) mixing the **liposome**-encapsulated **antigen** with (C), and
(c) optionally adding (A) if **antigen/adjuvant** complex is not used in step (a).
USE - As a vaccine composition (claimed).
ADVANTAGE - The composition provides effective long-term immunocontraception in a mammal. The composition is free of lipid A. The composition potentiates and enhances an immune response in an animal. A single dose of the composition provides long-term immune response in a variety of species, typically not requiring boosters. The **antigen** used elicits an antibody that recognizes a native epitope in mammals such as horse, rabbit, deer and cat.
Dwg.0/1

=> d bib ab 1-61 l16

L16 ANSWER 1 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2003-402921 [38] WPIDS
DNN N2003-321461 DNC C2003-107147
TI Composition useful for enhancing the immunogenicity of veterinary vaccine comprises an immunomodulator and an immunoadjuvant.
DC A96 B04 C06 D16 P32
IN CHU, H
PA (AMHP) WYETH
CYC 100

PI WO 2003024354 A2 20030327 (200338)* EN 21p
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
ADT WO 2003024354 A2 WO 2002-US29229 20020913
PRAI US 2002-243075 20020912; US 2001-322840P 20010917
AB WO2003024354 A UPAB: 20030616
NOVELTY - A composition (C1) comprising an immunomodulator and an immunoadjuvant, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for an improved veterinary vaccine composition (C2) comprising an **antigen**, an immunomodulator, an immunoadjuvant and a carrier.
ACTIVITY - None given.
MECHANISM OF ACTION - Vaccine.
No biological data given.
USE - The composition is useful for enhancing the immunogenicity of a veterinary vaccine; for potentiating, accelerating or extending the immunogenicity of a weak, immunosuppressive or marginally safe **antigen** (all claimed).
ADVANTAGE - The composition improves the immunological response of an animal to the **antigen** when administered concurrently or in admixture with vaccine composition. The composition improves the immunogenicity and efficacy of animal vaccines without raising toxicity concerns. The composition provides highly unique vaccine possessing significantly improved immunogenicity in mammals and birds by inducing a stronger stimulation on cell-mediated immunity including T memory cells and to provide a longer duration of immunity by requiring smaller or less frequent dosages of antigens over time and lessening side effects or potential for toxicity.
Dwg.0/0

L16 ANSWER 2 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2003194082 EMBASE
TI The domain III fragment of Japanese encephalitis virus envelope protein: Mouse immunogenicity and **liposome** adjuvanticity.
AU Wu S.-C.; Yu C.-H.; Lin C.-W.; Chu I.-M.
CS S.-C. Wu, Department of Life Science, Institute of Biotechnology, National Tsing Hua University, Hsinchu 30013, Taiwan,Province of China. scwu@life.nthu.edu.tw
SO Vaccine, (2 Jun 2003) 21/19-20 (2516-2522).
Refs: 20
ISSN: 0264-410X CODEN: VACCDE
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB The E protein of Japanese encephalitis virus (JEV) is the major **antigen** used to elicit neutralizing antibody response and protective immunity in hosts. In this study, the domain III protein of the attenuated strain CH2195LA was cloned to the pET32a expression vector and expressed as a thioredoxin (Trx) fusion protein in Escherichia coli. The recombinant protein was unique in forming a large fraction of the soluble recombinant protein in E. coli. The purified domain III fusion protein (TrxD3) was emulsified in Freund's **adjuvant** (FA) as well as in different charged **liposomes** for immunization in mice. Immunization of TrxD3 fusion protein emulsified in Freund's

adjuvant and only the cationic **liposome** resulted in eliciting neutralizing antibodies and protective immunity in ICR mice. The cationic **liposome** can serve not only as a safer but also an effective **adjuvant** for the TrxD3 protein immunization. These studies can provide useful information for further developing the domain III recombinant protein vaccine against JEV.

L16 ANSWER 3 OF 61 EMBASE
AN 2003046336 EMBASE
TI **Liposomes** and ISCOMs.
AU Kersten G.F.A.; Crommelin D.J.A.
CS G.F.A. Kersten, Laboratory for Prod./Proc. Devmt., Natl. Inst. of Pub. Hlth./the E., P.O. Box 1, 3720 BA Bilthoven, Netherlands. gideon.kersten@rivm.nl
SO Vaccine, (14 Feb 2003) 21/9-10 (915-920).
Refs: 30
ISSN: 0264-410X CODEN: VACCDE
PUI S 0264-410X(02)00540-6
CY United Kingdom
DT Journal; Conference Article
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB **Liposomes** and ISCOMs have a long history as vehicles for **antigen** delivery. **Liposomes** can carry both membrane associated antigens as well as water soluble molecules. Their physical properties are highly variable, depending on composition and manufacturing method. This allows optimised design for specific tasks (targeting, co-incorporation of adjuvants, etc.). ISCOMs already have a build-in **adjuvant**, Quillaja saponin, which is a structural part of the vehicle. In recent years, considerable progress has been achieved with respect to the use of better defined saponin. Clinical trials with ISCOMs are in progress and registered **liposomal** vaccines exist. Here, follows a brief overview on recent developments with emphasis on pharmaceutical aspects.

L16 ANSWER 4 OF 61 EMBASE
AN 2003220506 EMBASE
TI Recent advances in veterinary vaccine adjuvants.
AU Singh M.; O'Hagan D.T.
CS M. Singh, Chiron Vaccines Research, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608, United States. manmohan_singh@chiron.com
SO International Journal for Parasitology, (2003) 33/5-6 (469-478).
Refs: 110
ISSN: 0020-7519 CODEN: IJPYBT
CY United Kingdom
DT Journal; General Review
FS 004 Microbiology
026 Immunology, Serology and Transplantation
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Next generation veterinary vaccines are going to mainly comprise of either subunit or inactivated bacteria/viruses. These vaccines would require optimal adjuvants and delivery systems to accord long-term protection from infectious diseases in animals. There is an urgent need for the development of new and improved veterinary and human vaccine adjuvants.

Adjuvants can be broadly divided into two classes, based on their principal mechanisms of action: vaccine delivery systems and 'immunostimulatory adjuvants'. Vaccine delivery systems are generally particulate e.g. emulsions, microparticles, ISCOMS and **liposomes**, and mainly function to target associated antigens into **antigen** presenting cells (APC). In contrast, immunostimulatory adjuvants are predominantly derived from pathogens and often represent pathogen associated molecular patterns, e.g. LPS, MPL and CpG DNA, which activate cells of the innate immune system. Recent progress in innate immunity is beginning to yield insight into the initiation of immune responses and the ways in which immunostimulatory adjuvants might enhance this process in animals and humans alike.

L16 ANSWER 5 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2003192790 EMBASE
TI Microparticles as vaccine adjuvants and delivery systems.
AU O'Hogan D.T.; Singh M.
CS Dr. D.T. O'Hogan, Vaccine Research, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608, United States. derek_o'hagan@chiron.com
SO Expert Review of Vaccines, (2003) 2/2 (269-283).
Refs: 169
ISSN: 1476-0584 CODEN: ERVXAX
CY United Kingdom
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Adjuvants can be broadly divided into two groups, based on their principal mechanisms of action: vaccine delivery systems and immunostimulatory adjuvants. Vaccine delivery systems are generally particulate (e.g., emulsions, microparticles, immunostimulatory complexes and **liposomes**) and function mainly to target associated antigens into **antigen**-presenting cells. However, increasingly, more complex formulations are being developed in which delivery systems are exploited both for the delivery of antigens and also for the delivery of coadministered immunostimulatory adjuvants. The rationale for this approach is to ensure that both **antigen** and **adjuvant** are delivered into the same population of **antigen**-presenting cells. In addition, delivery systems can focus the effect of the adjuvants onto the key cells of the immune system and limit the systemic distribution of the **adjuvant**, to minimize its potential to Induce adverse effects. The formulation and delivery of potent adjuvants in microparticles may allow the development of prophylactic and therapeutic vaccines against cancers and chronic Infectious diseases, which are currently poorly controlled. In addition, microparticle formulations may also allow vaccines to be delivered mucosally.

L16 ANSWER 6 OF 61 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 1
AN 2002-454763 [48] WPIDS
DNC C2002-129354
TI Composition useful as vaccine comprises carrier, **liposome**, **antigen** and **adjuvant**.
DC B04 C03 D16
IN BROWN, R G; KIMMINS, W C; POHAJDAK, W
PA (BROW-I) BROWN R G; (KIMM-I) KIMMINS W C; (POHA-I) POHAJDAK W; (IMMU-N) IMMUNOVACCINE TECHNOLOGIES INC
CYC 98
PI WO 2002038175 A1 20020516 (200248)* EN 66p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002110568 A1 20020815 (200256)
AU 2002014861 A 20020521 (200260)
ADT WO 2002038175 A1 WO 2001-CA1530 20011031; US 2002110568 A1 Provisional US 2000-246075P 20001107, Provisional US 2001-307159P 20010724, US 2001-992149 20011106; AU 2002014861 A AU 2002-14861 20011031
FDT AU 2002014861 A Based on WO 200238175
PRAI US 2001-307159P 20010724; US 2000-246075P 20001107; US 2001-992149 20011106
AB WO 200238175 A UPAB: 20020730
NOVELTY - A composition (I) comprises a carrier (C), **liposomes**, an **antigen** and an **adjuvant** (A). (C) comprises a continuous phase of hydrophobic substance.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the following:
(1) preparing (I) involving:
(a) encapsulating an **antigen** or an **antigen/adjuvant** complex in **liposomes** to form **liposome**-encapsulated **antigen**;
(b) mixing the **liposome**-encapsulated **antigen** with (C), and
(c) optionally adding (A) if **antigen/adjuvant** complex is not used in step (a).
USE - As a vaccine composition (claimed).
ADVANTAGE - The composition provides effective long-term immunocontraception in a mammal. The composition is free of lipid A. The composition potentiates and enhances an immune response in an animal. A single dose of the composition provides long-term immune response in a variety of species, typically not requiring boosters. The **antigen** used elicits an antibody that recognizes a native epitope in mammals such as horse, rabbit, deer and cat.
Dwg.0/1

L16 ANSWER 7 OF 61 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 2
AN 2002-499992 [53] WPIDS
DNC C2002-141547
TI **Adjuvant** composition useful in vaccine composition for use in medicine, comprises combination of immunostimulatory oligonucleotide and tocol.
DC B02 B04 D16
IN GARCON, N; GERARD, C M G; STEPHENNE, J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 97
PI WO 2002032454 A1 20020425 (200253)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002021689 A 20020429 (200255)
ADT WO 2002032454 A1 WO 2001-EP11985 20011016; AU 2002021689 A AU 2002-21689 20011016
FDT AU 2002021689 A Based on WO 200232454
PRAI GB 2000-25577 20001018
AB WO 200232454 A UPAB: 20020820
NOVELTY - An **adjuvant** composition (I) comprising a combination of an immunostimulatory oligonucleotide (Ia) and a tocol (Ib), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a vaccine composition (II) comprising (I), and an **antigen**

or antigenic composition;

(2) shifting (M1) the quality of an immune response against an **antigen**, generated by a vaccine comprising an immunostimulatory oligonucleotide, towards a Th1-type immune response, by formulating the vaccine with (Ia) and (Ib); and

(3) manufacturing a vaccine formulation, by formulating an oil in water **emulsion** comprising a tocol, admixing the tocol **emulsion** with an immunostimulatory oligonucleotide to form an **adjuvant**, and formulating the **adjuvant** with an **antigen** or antigenic composition.

ACTIVITY - Antiallergic; Antibacterial; Antifungal; Virucide; Cytostatic; Antiarteriosclerotic; Nootropic; Neuroprotective; Anti-HIV; Tuberculostatic; Hepatotropic.

MECHANISM OF ACTION - Vaccine (claimed). A range of **adjuvant** formulations with **antigen** (a fusion of the extracellular domain of Her2Neu linked to the phosphorylation domain (ECD-PD) were investigated. Groups 1-11 were treated with **adjuvant** formulations comprising the following 11 adjuvants and 25 micro g of **antigen**. The adjuvants include phosphate buffered saline (PBS); **liposomes** with QS21 and 3D-MPL in membrane; tocol containing oil in water **emulsion** with QS21 and 3D-MPL; CpG; **liposomes** with QS21 and 3D-MPL in membrane + CpG; tocol containing oil in water **emulsion** with QS21 and 3D-MPL + CpG; 3D-MPL + CpG; QS21 + CpG; tocol containing oil in water **emulsion** + CpG; **liposomes** with QS21 in membrane + CpG; and **liposomes** with 3D-MPL in membrane + CpG. Groups of B6F1 mice were vaccinated on four occasions, intramuscularly, 14 days apart. Fourteen days post the 4th vaccine dose, the mice were challenged subcutaneously with 2 multiply 10 to the power of 6 TC1 tumor cell expressing the Her2Neu. The size of the individual tumors were measured twice a week and expressed as a group mean. The results were shown graphically. Formulations comprising tocol and CpG induced a complete regression of the tumor.

USE - (II) is useful for treating an individual susceptible to or suffering from a disease, and in medicine (claimed). (I) is useful in vaccine. (I) is useful for immunoprophylaxis of diseases, and also for immunotherapy of diseases such as persistent viral, bacterial or parasitic infections, or chronic disorders, such as cancer. (II) is useful in prophylaxis or therapy of allergy, chronic disorders or diseases such as atherosclerosis and Alzheimer's disease, and persistent infections. (II) is particularly suitable for the immunotherapy of infectious diseases such as tuberculosis, AIDS and hepatitis B virus infections.

Dwg.0/10

L16 ANSWER 8 OF 61 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 3
AN 2002-471376 [50] WPIDS
CR 2000-687101 [67]
DNC C2002-134015
TI Immunogenic composition useful for treating patients suffering from cancer comprising cancer antigens e.g., MAGE, prostase, along with **adjuvant** combination comprising immunostimulatory oligonucleotide and saponin.
DC B04 D16
IN GARCON, N; GERARD, C M G; STEPHENNE, J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 97
PI WO 2002032450 A2 20020425 (200250)* EN 49p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002044337 A 20020429 (200255)

ADT WO 2002032450 A2 WO 2001-EP11984 20011016; AU 2002044337 A AU 2002-44337 20011016

FDT AU 2002044337 A Based on WO 200232450

PRAI US 2000-690921 20001018; GB 2000-25573 20001018; GB 2000-25574 20001018

AB WO 200232450 A UPAB: 20030429

NOVELTY - New Immunogenic composition (I) comprises:

(a) a cancer **antigen** (CA) e.g. MAGE or prostase antigens linked to heterologous fusion partner, prostase fragments comprising at least 20 amino acids of prostase, mutated prostase, P501S, Cripto, or Her2-neu derivatives devoid of substantial portion of Her-2 neu transmembrane domain, and

(b) **adjuvant** comprising saponin and immunostimulatory oligonucleotide.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of a combination of a saponin and immunostimulatory oligonucleotide and a CA in the manufacture of a medicament for the treatment or prophylaxis of tumors.

ACTIVITY - Cytostatic; antimicrobial; antiallergic; immunosuppressive.

MECHANISM OF ACTION - Vaccine.

A range of **adjuvant** formulations with the **antigen** which was a fusion of the extracellular domain of Her 2 neu linked to the phosphorylation domain (ECD-PD) (ECD-PD with no **adjuvant** (group 1) and ECD-PD with **liposomes** with QS21 and with any of the **adjuvant** combinations 3D-MPL in membrane, tocol containing oil in water **emulsion** with QS21 and 3D-MPL CpG, **liposomes** with QS21 and 3D-MPL in membrane +CpG, tocol containing oil in water **emulsion** with QS21 and 3D-MPL+CpG, 3D-MPL+CpG, QS21+CpG, tocol containing oil in water **emulsion**+CpG, **liposomes** with QS21 in membrane+CpG, **liposomes** with 3D-MPL in membrane+CpG (groups 2-11, respectively)) which was produced in Chinese hamster ovary (CHO) cells according to the methods of WO 00/44899, was investigated. Groups of B6F1 mice were vaccinated on four occasions (in 50 mu l volumes), intramuscularly, 14 days apart. 14 days post the 4th vaccine dose, the mice were challenged subcutaneously with 2 x 106 TC1 tumor cell expressing the Her 2 neu. The Her 2 neu-TC1 tumor cell lines was produced by transduction of TC1 cells by retroviral vectors coding for Her 2 neu. After a selection period with blastocydin, resistant clones were isolated and screened by fluorescence activated cell sorting (FACS) for Her 2 neu expression. The clone with the highest Her 2 neu expression was selected, and the challenge dose of 2 x 106 was identified to have a similar kinetic of growth as the wild-type TC1 cells and to give rise to a developing tumor in 100% of the control animals. The only vaccines that induced a complete regression of the tumor were vaccine containing both an immunostimulatory oligonucleotide and a saponin. The **adjuvant** tested (AS1, AS2, AS7) had similar effect. However, the combination of AS1 and AS7 or AS2 and AS7 were more effective adjuvants. Cell-mediated immune response (CMI) was clearly shown after 4 vaccinations in animals receiving the combined **adjuvant** on the whole molecule ECD-PD, but also on each part separately (ECD and ICD). The formulations were very effective in inducing tumor regression.

USE - (I) is useful for treating a patient suffering from susceptible to a cancer expressing a Her 2 neu or prostate specific/tumor **antigen**. (I) is also useful for treating a patient suffering from or susceptible to a cancer expressing any of MAGE, prostase, P501S or Cripto (claimed).

The formulations containing tumor antigens are useful for immunotherapeutic treatment of prostate, breast, colorectal, lung, pancreatic, renal, or melanoma cancers. (I) is useful for inducing an immune response in an individual, and for treating a mammal susceptible to or suffering from an infectious disease or cancer, or allergy or autoimmune disease. (I) is useful as a medicament.

ADVANTAGE - The immunostimulatory oligonucleotides (CpG) and saponin and optionally a lipopolysaccharide combination are extremely potent adjuvants. The oligonucleotides in the **adjuvant** and vaccine compositions act synergistically with the combined saponin/lipopolysaccharide in the induction of **antigen** specific immune responses leading to enhanced tumor regression. The formulations are potent in the induction of immune responses conventionally associated with Th-1 type immune system. Her 2 neu antigens that are formulated with 3D-MPL, QS21 and CpG oligonucleotide together with **liposome** or oil-in-water **emulsion** carrier, produce both a humoral and cell mediated response in comparison to the formulations containing only CpG that do not produce a significant cell-mediated immune response. Dwg.0/14

L16 ANSWER 9 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-362308 [39] WPIDS
CR 2002-351845 [38]
DNC C2002-102545
TI Novel immunogenic composition comprising Streptococcus pneumoniae polysaccharide and protein **antigen** useful for preventing, ameliorating and treating pneumococcal infections in infants, toddlers and elderly persons.
DC B04 D16
IN LAFERRIERE, C A J; POOLMAN, J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA
CYC 98
PI WO 2002022167 A2 20020321 (200239)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002020548 A 20020326 (200251)
EP 1317279 A2 20030611 (200339) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002022167 A2 WO 2001-EP10568 20010912; AU 2002020548 A AU 2002-20548 20010912; EP 1317279 A2 EP 2001-984626 20010912, WO 2001-EP10568 20010912
FDT AU 2002020548 A Based on WO 200222167; EP 1317279 A2 Based on WO 200222167
PRAI GB 2000-22742 20000915
AB WO 200222167 A UPAB: 20030619
NOVELTY - An immunogenic composition (I) comprising at least one Streptococcus pneumoniae polysaccharide **antigen** and at least one S. pneumoniae protein **antigen** selected from PhtA, PhtD, PhtB, PhtE, SpsA, LytB, LytC, LytA, Sp125, Sp101, Sp128, Sp130 and Sp133, or its immunologically functional equivalent, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine (II) comprising (I); and

(2) making (I) involves selecting one or more pneumococcal polysaccharide **antigen**(s) and one or more pneumococcal protein **antigen**(s), and mixing the polysaccharide and protein antigens with a suitable excipient.

ACTIVITY - Auditory; antiinflammatory.

No biological data is given.

MECHANISM OF ACTION - Vaccine (claimed); inducer of T-cell mediated response against pneumococcal disease.

The impact of the addition of a Streptococcus pneumoniae protein plus or minus 3D-MPL **adjuvant** on the protective effectiveness of protein D (PD)-conjugated 11-valent polysaccharide vaccine against pneumococcal lung colonization in OF1 mice intranasally challenged with

serotype 2, 4 or 6B was tested. The prophylactic efficacy of a vaccine containing the 11-valent polysaccharide-protein D conjugate, a S. pneumoniae protein and AlPO4+3D-MPL adjuvants, was compared to the classical AlPO4 adsorbed 11-valent polysaccharide-protein D conjugate formulation. Groups of 12 female 4 week old OF1 mice were immunized subcutaneously, with formulations containing 50 mu g AlPO4, 0.1 mg PS/serotype of PD-conjugated 11-valent polysaccharide vaccine + 50 mu g AlPO4, or 0.1 mu g PS/serotype of PD-conjugated 11-valent polysaccharide vaccine + 10 mu g S. pneumoniae protein + 50 mu g AlPO4 + 5 mu g 3D-MPL. Challenge was done at day 21 as a significant protection was conferred by the 11-valent polysaccharide conjugate vaccine supplemented with the S. pneumoniae protein and adjuvanted with AlPO4+MPL. On the contrary, no significant protection was observed in animals immunized with the 11-valent polysaccharide conjugate/AlPO4 formulation. This result proved that the addition of the protein and 3D-MPL **adjuvant** enhanced the effectiveness of the 11-valent polysaccharide conjugate vaccine against pneumonia.

USE - (I) is useful as a medicament. (II) is useful for preventing or ameliorating S. pneumoniae infection in a patient over 55 years, or in the manufacture of a medicament for the prevention or treatment of pneumonia in a patient over 55 years. (I) or (II) is useful in the manufacture of a medicament for preventing, ameliorating or treating otitis media in infants or toddlers (claimed).

Dwg.0/0

L16 ANSWER 10 OF 61 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 2003-07170 BIOTECHDS
TI Recovering immunogenic outer membrane associated polypeptides from microbial cells, useful for inducing passive or active immunization against bacterial, fungal or protozoan infection, comprises culturing cells in iron-starved conditions;
recombinant protein production and antibody for use in disease therapy
AU SCOTT D L; THOMAS C B; SMALLS F; WILLIAMS M
PA D-SQUARED BIOTECHNOLOGIES INC
PI WO 2002083843 24 Oct 2002
AI WO 2002-US11110 10 Apr 2002
PRAI US 2001-304390 10 Jul 2001; US 2001-282809 10 Apr 2001
DT Patent
LA English
OS WPI: 2003-067575 [06]
AB DERWENT ABSTRACT:

NOVELTY - Recovering immunogenic outer membrane associated polypeptides (OMAPs) from microbial cells comprises: (a) culturing microbial cells or bacterial cells in iron-starved conditions to up-regulate OMAPs; (b) harvesting membranes from cells, and solubilizing (bacterial) membrane proteins; (c) purifying OMAPs from contaminating immunosuppressive endotoxins; and (d) purifying OMAPs from their binding ligands.

DETAILED DESCRIPTION - Recovering immunogenic outer membrane associated polypeptides (OMAPs) from microbial cells comprises: (a) culturing microbial cells or bacterial cells in iron-starved conditions to up-regulate OMAPs; (b) harvesting membranes from cells, and solubilizing (bacterial) membrane proteins; (c) purifying OMAPs from contaminating immunosuppressive endotoxins; and (d) purifying OMAPs from their binding ligands. The purified OMAPs from the microbial cells are substantially endotoxin-free and ligand-free, and are capable of generating an OMAP specific immunoresponse when injected into a host. The OMAPs comprise the Scott-Thomas domain and the D2 domain, where the D2 domain is selected from the group of D2 domain 1, D2 domain 3, or D2 domain 4. INDEPENDENT CLAIMS are also included for the following: (1) Isolated nucleotide sequence that encodes an epitope of FptA that contains a siderophore binding site; (2) Producing (M1) anti-OMAPs antibody; (3) Vaccine for immunizing an animal against microbial infection comprising a non-iron-regulated OMAP recovered by M1, and a

physiologic carrier; (4) Immunizing (M2) an animal against a bacterial infection; (5) Diagnostic kits for detecting OMAPs in a biological sample comprising: (a) primer pair for amplifying a nucleic acid, where the oligonucleotide primers are at least 14 bases in length; or (b) oligonucleotide probe that binds under high stringency conditions to the isolated nucleic acid cited above; and (c) containers for each of the primers, or for the probe; (6) Recovering (M3) OMAPs from fungi, gram-negative bacteria and gram-positive bacteria species; (7) Actively immunizing (M4) a host animal or human using OMAPs of (6) for the recovery of surface exposed immunogenic polypeptides from gram-negative bacteria and gram-positive bacteria species; (8) Inducing (M5) passive immunization of a host, where one or more surface exposed immunogenic fragments comprising any one of 15 sequences consisting of 19-350 amino acids fully defined in the specification, generate specific antibodies in an animal or human and provide prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species; and (9) Preventing (M6) or treating wound infections or sepsis caused by gram-negative and gram-positive bacteria species.

BIOTECHNOLOGY - Preferred Methods: Recovering immunogenic OMAPs from microbial cells comprises: (a) culturing the microbial cells in iron-starved condition to up-regulate OMAPs, where the OMAPs are preferably comprised of D2 domain 4;(b) purifying OMAPs from contaminating immunosuppressive endotoxins; and (c) further purifying OMAPs from their binding ligands. The D2 domains 1, 3 and 4 comprise a fully defined sequence of 97, 428 and 82 amino acids, respectively, given in the specification. Particularly, recovering immunogenic OMAPs from Stenotrophomonas maltophilia strain comprises: (a) culturing the S. maltophilia strain in iron-starved conditions to up-regulate OMAPs; (b) harvesting membrane from S. maltophilia, and solubilizing the membrane proteins; (c) purifying OMAPs from contaminating immunosuppressive endotoxins; and (d) further purifying OMAPs from their binding ligands; where the purified OMAPs from S. maltophilia are substantially endotoxin-free and ligand-free, and are capable of generating an OMAP specific immunoresponse when injected into a host. Recovering OMAPs from fungi, gram-negative bacteria and gram-positive bacteria species comprises: (a) propagation of fungi, gram-negative bacteria and gram-positive bacteria species in condition of low iron; (b) separation of membrane associated polypeptides, including receptors for iron-binding molecules (i.e. siderophore receptors) that are complexed with there iron-binding ligands, from other components of the cell wall of either gram-negative and gram-positive bacteria species; and (c) separation of siderophore receptors from their iron-binding ligands. M1 comprises: (a) culturing from bacteria, fungi, or protozoans cells, e.g. S. maltophilia cells, in iron-starved condition to up-regulate OMAPs; (b) purifying OMAPs from contaminating immunosuppressive endotoxins and ligands; (c) generating antisera by using purified OMAPs to animals; (d) purifying anti-OMAPs immunogobulins; and (e) characterizing the anti-OMAPs. M1 further comprises producing anti-OMAP Fab fragments by separating IgG molecules into Fab and Fc fragments. M2 comprises administering the vaccine of (3). The vaccine induces an immunologically effective antibody titer in the host to prevent or eliminate the infection without administration of a booster of the vaccine. M4 comprises actively immunizing a vertebrate animal with gram negative and gram positive bacteria species comprising actively immunizing a vertebrate animal with gram-negative and gram-positive species membrane associated polypeptides, where the amount of the membrane associated polypeptides in a carrier is about 25-5000 microg/ml. M4 comprises: (a) isolating and purifying gram-negative and gram-positive bacteria species genomic DNA which is cloned into an appropriate vector and used to produced a cDNA expression library; (b) isolating and purifying gram-negative and gram-positive bacteria species membrane associated polypeptides antisera is used to probe expression library for surface exposed immunogenic polypeptides; (c) isolating and characterizing gram-negative and gram-positive bacteria

species surface exposed immunogenic polypeptides; (d) identifying the surface exposed immunogenic polypeptides which possess sequence motifs comprising the sequences of 97, 428, and 82 amino acids fully defined in the specification; and (e) classifying and identifying epitopes in receptors of iron-binding ligands that are conserved amongst gram-negative, gram-positive and gram-negativegram-positive bacteria species comprising 15 sequences consisting of 19-350 amino acids fully defined in the specification. The polypeptide or the immunogenic fragment produces an antibody response in an animal or human singly or in combination for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. The carrier, which is a physiologic carrier, is a liquid, and the amount of the surface exposed immunogenic polypeptide(s) in the vaccine is about 25-5000 microg/ml. M5 comprises: (a) immunizing laying hens with immunogenic polypeptides or immunogenic fragments comprising any one of 15 sequences consisting of 19-350 amino acids fully defined in the specification; (b) recovering the anti- bacterial polyclonal antibodies from the egg yolks; and (c) purifying the polyclonal antibodies. The method uses one or more anti-bacterial monoclonal antibodies for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. Transgenic mice capable of producing high affinity human anti-bacterial mononclonal antibodies are also immunized using the method above. The method uses one or more anti-bacterial single-chain Fv (scFv) monoclonal antibodies for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. M5 comprises: (a) immunoglobulin genes from anti-bacterial monoclonal cell lines are cloned into an appropriate expression vector to produce scFv; (b) the anti-bacterial scFv monoclonal antibodies are generated; and (c) the monoclonal antibodies are administered for the prophylaxis or treatment of disease and infection caused by gram-negative and gram-positive bacteria species. The anti-bacterial scFv monoclonal antibodies are also administered for neutralization of gram-negative and gram-positive bacteria species in a carrier. Preventing or treating wound infections or sepsis caused by gram-negative and gram-positive bacteria species by administering to an animal or human, the anti-bacterial polyclonal antibodies of (8) for the effective neutralization of gram-negative and gram-positive bacteria species in a carrier. Preferred Vaccine: The vaccine stimulates the production of antibody to the OMAPs in an adult animal. The vaccine induces an immunologically effective antibody titre in the host to prevent or eliminate the infection without administration of a booster of the vaccine. The carrier is physiological saline, phosphate-buffered saline, Tris (hydroxymethyl aminomethane), or Tris-buffered saline. The carrier is in the form of a solution, water-in-oil **emulsion**, **liposomes**, or a metabolizable solid matrix. The vaccine further comprises an **adjuvant** selected from the group of aluminum hydroxide, aluminum phosphate, or Freund's Incomplete **Adjuvant**. Preferred Cells: The microbial cells are selected from the group of bacteria, fungi, or protozoans, such as S. maltophilia, Bacillus cepcia, Cryptococcis neoformans, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus or Staphylococcus epidermidis. The microbial cells or bacteria can also be gram-negative bacteria, gram-positive bacteria, or mycobacteria.

~~ACTIVITY--~~Antibacterial; Fungicide; Protozoacide; Immunostimulant. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The methods are useful for recovering immunogenic OMAPs for inducing passive or active immunization against bacterial, fungal or protozoan infections. The antibodies are useful for diagnosing, preventing and treating bacterial, fungal or protozoan infections (claimed).

ADMINISTRATION - Loading dose is about 2.5 mg/kg. The vaccine is administrated by subcutaneous injection, intramuscular injection,

sustained release repository, aerosolization, or inoculation into an egg (all claimed). Administration of the antibodies may be intravenous, subcutaneous, intramuscular, intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation.

EXAMPLE - An overnight culture of Stenotrophomonas maltophilia strain, designated D2-DLS01 was used to inoculate 500 ml of freshly prepared M9-minimal medium supplemented with maltose (10 g/ml), methionine (40 microg/ml), 1 M MgSO4 (0.1%), and the iron chelator 2'2' dipyridyl (100 microM). The cells were concentrated by centrifuging the culture. The concentrated bacteria were resuspended in 17 ml of HE buffer in a 50 ml sterile tube, then frozen in liquid nitrogen and thawed at room temperature. This step was repeated until the solution became viscous. Ten milliliters of the viscous lysate was layered to differentiate the cytoplasmic and membrane fractions and analyzed for iron reactive material and the presence of lipopolysaccharide (LPS). The iron reactivity and the LPS contamination were localized to the membrane fraction. The membrane fraction was resuspended in 50 ml of solubilization buffer and incubated for 1 hour at 4degreesC. The solubilized membranes were mixed with 10% polyethyleneimine (PEI). The iron reactivity was identified in the PEI supernatant while the LPS contamination molecules were localized to the PEI pellet. The iron reactive PEI supernatant (50 ml) was mixed by slow stirring with 18.05 g of ammonium sulfate and incubated with continuous stirring at 4degreesC for 1 hour. The iron-reactive fraction was recovered in the ammonium sulfate pellet, no LPS was detectable. The ammonium sulfate precipitate was resuspended in 25 ml of HE buffer and size fractionated by tangential-flow ultra centrifugation. The filtrate and retainate were analyzed for iron reactivity using the CAS assay and for the presence of LPS. The iron reactivity was found in the retainate, no LPS were detected in either fraction. The iron reactivity was transferred to the filtrate by the addition of solid urea to a final concentration of 6 M. The retainate, for D2-DLS01 **antigen** cocktail, was modified with 0.02% sodium azide and stored at -20degreesC. (91 pages)

L16 ANSWER 11 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 4
AN 2002230024 EMBASE
TI Recent advances in vaccine adjuvants.
AU Singh M.; O'Hagan D.T.
CS M. Singh, Immunology and Infectious Diseases, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608, United States. manmohan_singh@chiron.com
SO Pharmaceutical Research, (2002) 19/6 (715-728).
Refs: 191
ISSN: 0724-8741 CODEN: PHREEB
CY United States
DT Journal; (Short Survey)
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB New generation vaccines, particularly those based on recombinant proteins and DNA, are likely to be less reactogenic than traditional vaccines but are also less immunogenic. Therefore, there is an urgent need for the development of new and improved vaccine adjuvants. Adjuvants can be broadly separated into two classes based on their principal mechanisms of action: vaccine delivery systems and immunostimulatory adjuvants. Vaccine-delivery systems generally are particulate (e.g, emulsions, microparticles, iscoms, and **liposomes**)and function mainly to target associated antigens into **antigen**-resenting cells. In contrast, immunostimulatory adjuvants are derived predominantly from pathogens and often represent pathogen-ssociated molecular patterns (e.g.,

lipopolysaccaride, monophosphoryl lipid A, CpG DNA), which activate cells of the innate immune system. Recent progress in innate immunity is beginning to yield insight into the initiation of immune responses and the ways in which immunostimulatory adjuvants may enhance this process. The discovery of more potent adjuvants may allow the development of prophylactic and therapeutic vaccines against cancers and chronic infectious diseases. In addition, new adjuvants may also allow vaccines to be delivered mucosally.

L16 ANSWER 12 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002417530 EMBASE
TI [Adjuvants for vaccines].
ADJUVANZIEN FUR IMPFSTOFFE.
AU Broker M.
CS Dr. M. Broker, Chiron Behring GmbH and Co, Postfach 1630, 35006 Marburg, Germany
SO Medizinische Monatsschrift fur Pharmazeuten, (1 Nov 2002) 25/11 (373-378). Refs: 13
ISSN: 0342-9601 CODEN: MMPHDB
CY Germany
DT Journal; (Short Survey)
FS 037 Drug Literature Index
039 Pharmacy
LA German

L16 ANSWER 13 OF 61 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 5
AN 2002-049090 [06] WPIDS
DNC C2002-013695
TI New non-peptide **antigen** from Mycobacterium tuberculosis, useful as a vaccine for eliciting or stimulating an immune against Mycobaterium tuberculosis, especially as a phophylactic or therapeutic treatment.
DC A96 B04 D16
IN BELTZ, G; COX, D; KENSIL, C; LECLAIR, K; LIU, G; BELTZ, J
PA (ANTI-N) ANTIGENICS INC; (BELT-I) BELTZ G; (COXD-I) COX D; (KENS-I) KENSIL C; (LECL-I) LECLAIR K; (LIUG-I) LIU G; (AQUI-N) AQUILA BIOPHARMACEUTICALS INC
CYC 95
PI WO 2001075096 A1 20011011 (200206)* EN 57p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001051316 A 20011015 (200209)
US 2002044951 A1 20020418 (200228)
ADT WO 2001075096 A1 WO 2001-US11016 20010404; AU 2001051316 A AU 2001-51316 20010404; US 2002044951 A1 Provisional US 2000-194519P 20000404, US 2001-825789 20010404
FDT AU 2001051316 A Based on WO 200175096
PRAI US 2000-194519P 20000404; US 2001-825789 20010404
AB WO 200175096 A UPAB: 20020128
NOVELTY - A non-peptide **antigen** (I) isolated and purified from Mycobacterium tuberculosis, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of enhancing an immune response in a mammal to Mycobacterium tuberculosis by administering a vaccine composition comprising (I);

(2) a vaccine composition comprising (I), where the vaccine enhances an immune response to M. tuberculosis in a mammal to which the vaccine is administered;

(3) a pharmaceutical composition comprising (I) and a vehicle;

(4) a vaccine composition comprising one or more non-peptide **antigen** isolated and purified from M. tuberculosis and at least one lipid carrier, where the vaccine comprises vesicles; and

(5) a method of making a vaccine composition comprising extruding a mixture of one or more lipid carriers, and one or more isolated non-peptide antigens through a filter membrane.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

USE - (I) is useful as vaccine component for stimulating or eliciting an immune response against Mycobacterium tuberculosis, especially as a therapeutic or prophylactic treatment.

Dwg.0/13

L16 ANSWER 14 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-114486 [15] WPIDS
DNC C2002-035220
TI Product for modulating or stimulating immune response comprises lipids having glycerol backbone with at least one alkyl or acyl chain e.g. phospholipid.
DC B04 B05 C03
IN PORTER, W L
PA (PORT-I) PORTER W L
CYC 97
PI WO 2001095914 A1 20011220 (200215)* EN 59p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001064079 A 20011224 (200227)
EP 1289530 A1 20030312 (200320) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001095914 A1 WO 2001-GB2568 20010613; AU 2001064079 A AU 2001-64079 20010613; EP 1289530 A1 EP 2001-938401 20010613, WO 2001-GB2568 20010613
FDT AU 2001064079 A Based on WO 200195914; EP 1289530 A1 Based on WO 200195914
PRAI GB 2000-28239 20001120; GB 2000-14437 20000614; GB 2000-26667 20001101
AB WO 200195914 A UPAB: 20020306
NOVELTY - Product comprises lipids having a glycerol backbone carrying at least one alkyl or acyl chain. The lipid is a phospholipid, glycolipid or a neutral lipid with 10-22C atoms in the hydrocarbon chain.

ACTIVITY - Immunostimulant; Immunomodulator.

In a test, chickens (age 1-21 days) received food supplemented with a 2:1 methanol/chloroform extract of Bacillus subtilis, at the rate of the extract obtained from 100 mg Bacillus subtilis dried biomass per kg of feed. The extract was applied to a dusty and finely granular preparation of expanded mica containing a high proportion of particles of 0.2-100 mu m before incorporating into the feed. The growth rate of treated chickens exceeded that of controls by 14.1%.

MECHANISM OF ACTION - None given in source material.

USE - Used for stimulating, modulating, promoting and/or modifying immune response in animals and humans, such as for suppressing rather than enhancing the immune response to antigenic stimulus e.g. in the control of immune diseases (all claimed). The product is used for enhancing or modulating the mucosal and systemic immune response to antigenic challenge for preventing and treating infectious and immune disease.

ADVANTAGE - The product facilitates access to the immune system to stimulate immunicity and/or to modulate the immune response to antigenic stimulus.

Dwg.0/15

L16 ANSWER 15 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-639105 [73] WPIDS
DNC C2001-189043
TI New amphipathic aldehyde containing compounds or their salts useful as adjuvants and immunoeffectors.
DC B05
IN JOHNSON, D A; JOHNSON, D
PA (JOHN-I) JOHNSON D A; (CORI-N) CORIXA CORP
CYC 96
PI WO 2001070663 A2 20010927 (200173)* EN 72p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2001053363 A1 20011220 (200206)
AU 2001045823 A 20011003 (200210)
EP 1265840 A2 20021218 (200301) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001070663 A2 WO 2001-US8548 20010316; US 2001053363 A1 Provisional US 2000-190466P 20000317, US 2001-810915 20010316; AU 2001045823 A AU 2001-45823 20010316; EP 1265840 A2 EP 2001-918784 20010316, WO 2001-US8548 20010316
FDT AU 2001045823 A Based on WO 200170663; EP 1265840 A2 Based on WO 200170663
PRAI US 2000-190466P 20000317; US 2001-810915 20010316
AB WO 200170663 A UPAB: 20011211
NOVELTY - Amphipathic aldehyde containing compounds or their salts are new.

DETAILED DESCRIPTION - Amphipathic aldehyde containing compound of formula (I) or its salts is new.

R = H or -C(O)H;

R1 = H, optionally substituted 1-20C alkyl, saccharyl (which is a mono- or disaccharide or glucuronic acid group) or a group of formula -C(O)-(C(R3)(R4))n-COOH;

R3 and R4 = H or optionally substituted 1-10C alkyl;

n = 1 - 5;

R2 = H, optionally substituted 1-20C alkyl or a group of formula -(CH2)mCH(OH)(CH2)pOR5;

m and p = 1 - 2;

R5 = optionally substituted 2-20C alkyl or a group of formula -C(O)-(CH2)j-CH(OC(O)(R6))-R7;

j = 1 - 5; and

R6 and R7 = H or optionally substituted 1-20C alkyl.

INDEPENDENT CLAIMS are also included for the following:

(1) a **liposome** vesicle comprising (I);

(2) a compound comprising an **antigen** covalently linked to (I);

(3) a vaccine composition comprising either (I), or the **antigen** and (I);

(4) an **adjuvant** composition for potentiating the immunogenicity of the **antigen** comprising a suspension of water or an aqueous solution containing (I); and

(5) preparing (I) involving contacting a first compound of formula (II) with a second compound of formula MXn, MgX2-OEt2, BX3.SMe2, Et2AlCl, EtAlCl2, monoalkyl boronhalide, dialkylboronhalide, monoaryl boronhalide or diaryl boronhalide to form a compound of formula (III) or its salt.

R8 = R2 (preferably methyl);

M = Al3+, As3+, B3+, Fe2+, Fe3+, Ga3+, Mg2+, Sb3+, Sb5+, Sn2+, Sn4+, Ti2+, Ti3+, Ti4+, Zn2+;

n = 2 - 5; and

X = Cl, I, F or Br.

ACTIVITY - Cytostatic; Immunosuppressive; Antibacterial; Antiviral; Antiallergic.

Methyl 4-(3-formyl-4-hydroxyphenoxymethyl) benzoate (isotucaresol methyl ester) (A) was evaluated for **adjuvant** activity with a model hepatitis B vaccine. (A) was prepared as an aqueous formulation with PBS and mixed with recombinant hepatitis B surface **antigen** (rHBsAg) with 2-((R)-3-tetradecanoyloxytetradecanoylamino)ethyl-2-deoxy-4-O-phosphono-3-O-((R)-3-tetradecanoyloxytetradecanoyl)-2-((R)-3-tetradecanoyloxytetradecanoylamino) beta -D-glucopyranoside triethylammonium salt (B) (**adjuvant**). (B) was solubilized in an aqueous formulation containing dipalmitoylphosphatidyl choline in water. A comparative formulation was prepared using (A) without (B). Five female mice were administered with the test/comparative vaccine in a dose of 500 micro g on 0 and 14 days by subcutaneous injection. The gross serum geometric serum titers were IGG = 100001 - 500000/25001 - 50000, IgG1 = 50001 - 75000/100001 - 500000, IgG2a = 100001 - 500000/1500 - 3000 and IgG2b = 25001 - 50000/1000 - 1500. The results obtained showed that each molecule mediated enhanced serum antibody production.

MECHANISM OF ACTION - None given.

USE - As an **adjuvant** and immunoeffector for inducing immunogenicity of the **antigen** in a mammal and for treating or preventing a disease in the mammal such as a human being, the disease includes cancer, autoimmune disease, allergy or an infectious disease such as bacterial or viral infection (all claimed).

ADVANTAGE - (I) boosts the protective immune response without inducing unwanted toxicity and pyrogenicity.

Dwg.0/0

L16 ANSWER 16 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-476107 [51] WPIDS
DNC C2001-142806
TI New pharmaceutical compositions, useful as vaccines for treating or preventing neurodegenerative disorders, e.g. Alzheimer's Disease, loss of cognitive function, senile dementia, Parkinson's disease or cerebral palsy.
DC B04 D16
IN SRIVASTAVA, P K
PA (UYCO-N) UNIV CONNECTICUT HEALTH CENT
CYC 22
PI WO 2001053457 A2 20010726 (200151)* EN 47p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU CA JP
AU 2001029592 A 20010731 (200171)
ADT WO 2001053457 A2 WO 2001-US1665 20010118; AU 2001029592 A AU 2001-29592 20010118
FDT AU 2001029592 A Based on WO 200153457
PRAI US 2000-489219 20000121
AB WO 200153457 A UPAB: 20010910
NOVELTY - A pharmaceutical composition, which comprises a pharmaceutical carrier and an immunogenic amount of an antigenic molecule for treating or preventing a neurodegenerative disorder, is new. The antigenic molecule displays the antigenicity of an **antigen** associated with a neurodegenerative disorder, with the proviso that the antigenic molecule is not beta amyloid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) recombinant cells transformed with:

(a) a nucleic acid comprising a sequence that is operably linked to a promoter, where the nucleic acid encodes a fusion protein that has an antigenic molecule operatively linked to a carrier protein, and where antigenic molecule displays the antigenicity of an **antigen** associated with a neurodegenerative disorder; or

(b) nucleic acid comprising either:

(i) a first nucleic acid having a first nucleotide sequence that is operably linked to a first promoter and encodes an antigenicity of an **antigen** associated with a neurodegenerative disorder, and

(ii) a second nucleic acid comprising a second nucleic acid sequence that is operably linked to a second promoter and encodes a carrier protein, such that the antigenic molecule and the carrier protein are expressed within the cell and non-covalently associate with each other to form a complex that in sufficient amount is capable of eliciting an immune response to the antigenic molecule;

(2) a method for preparing a fusion protein capable of eliciting an immune response against a neurodegenerative disorder comprising:

(a) culturing the recombinant cell; and

(b) recovering the fusion protein from the cells;

(3) a method of mixing the carrier with one or more antigenic molecules in vitro, where one or more antigenic molecules display the antigenicities of antigens associated with a neurodegenerative disorder, comprising:

(a) incubating the antigenic molecule or molecules with a carrier protein for formation of the complex; and

(b) isolating the complexes;

(4) a method for eliciting an immune response against an **antigen** associated with a neurodegenerative disorder in an individual by administering to the individual the antigenic molecule that displays the antigenicity of an **antigen** associated with a neurodegenerative disorder; and

(5) methods of treating or protecting against a neurodegenerative disorder in an individual having a neurodegenerative disorder, or in whom prevention of a neurodegenerative disorder is desired, comprising administering to the individual the composition or the fusion protein cited above.

ACTIVITY - Neuroprotective; nootropic; neuroleptic; cerebroprotective; antiparkinsonian; anticonvulsant.

No details of clinical tests are given.

MECHANISM OF ACTION - Vaccine.

USE - The pharmaceutical composition is useful for treating or preventing neurodegenerative disorders. The neurodegenerative disorders include Alzheimer's Disease, age-related loss of cognitive function, senile dementia, Parkinson's disease, amyotrophic lateral sclerosis, Wilson's Disease, cerebral palsy, progressive supranuclear palsy, Guam disease, Lewy body dementia, prion diseases, spongiform encephalopathies, Creutzfeldt-Jakob disease, polyglutamine diseases, Huntington's disease, myotonic dystrophy, Freidrich's ataxia, Gilles de la Tourette's syndrome, seizure disorders, epilepsy, chronic seizure disorder, stroke, brain trauma, spinal cord trauma, AIDS dementia, alcoholism, autism, retinal ischemia, glaucoma, autonomic function disorder, hypertension, neuropsychiatric disorder, schizophrenia or schizoaffective disorder (all claimed). The pharmaceutical composition is particularly useful as vaccines for treating or preventing the diseases cited above.

Dwg.0/0

L16 ANSWER 17 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-398076 [42] WPIDS
DNC C2001-121056
TI Novel vaccine composition useful for treatment or prophylaxis of toxoplasmosis infections, comprises toxoplasma protein, SAG3, its immunogenic derivative, or a truncated toxoplasma protein.
DC B04 D16
IN BIEMANS, R; BOLLEN, A; DE NEVE, J; HAUMONT, M; JACQUET, A
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 94
PI WO 2001043768 A2 20010621 (200142)* EN 45p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001031588 A 20010625 (200162)

ADT WO 2001043768 A2 WO 2000-EP12704 20001212; AU 2001031588 A AU 2001-31588 20001212

FDT AU 2001031588 A Based on WO 200143768

PRAI GB 1999-29434 19991213

AB WO 200143768 A UPAB: 20010726

NOVELTY - A vaccine composition (I) comprising toxoplasma protein, SAG3 with a sequence (S) comprising 385 amino acids fully defined in the specification, or its immunogenic derivative, or comprising a truncated toxoplasma protein which comprises amino acid residues 40-359 of (S) or its immunogenic derivative, in combination with a suitable **adjuvant** and/or carrier, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a SAG3 protein (II) of a sequence (S), or its immunogenic derivative; and

(2) a DNA sequence (III) comprising 1446 base pairs fully defined in the specification, encoding (II).

ACTIVITY - Protozoacide.

Guinea pigs were immunized with recombinant SAG3 formulated with an **adjuvant** comprising 3D-MPL and a non-reactogenic form of QS21, or the **adjuvant** alone. After immunization, animals were bled and sera were tested for the presence of anti-SAG3 IgG antibodies. Before **antigen** injection, all guinea pigs were monitored for absence of seroreactivity against Toxoplasma. Females were mated with males for breeding after immunization, and infected using 5.105 tachyzoites. Infectious status of pups delivered from guinea pigs was evaluated in a mouse assay, pups were sacrificed within 48 hours following delivery, each brain was homogenized in phosphate buffered saline (PBS) and injected into two female BalbC mice. Mice that did not survive from 21 days onwards after brain homogenate injection were considered infected and their mortality indicated the infection status of the pups. In was assessed that a pup was infected once one of the two injected mice died. After challenge, 15 SAG3 and 16 mock-immunized guinea pigs produced respectively 52 and 58 pups of which 4 and 20 respectively were excluded for further analysis because, as stillborn pups or pups retrieved from dead mother were always negative in the mouse assay even if they originated from the mock-immunized group, probably due to parasite inactivation. After exclusion, 48 and 38 pups, originated from 15 and 11 litters respectively, were analyzed. Protection against vertical transmission was observed. The results showed that the proportion of infected pups were less in SAG3 immunized group when compared to the mock-immunized group.

MECHANISM OF ACTION - Vaccine (claimed).

USE - (I) is useful in medical therapy, for treatment or prophylaxis of toxoplasmosis infections. (I) is useful in the prevention of both horizontal and vertical (congenital) transmission of toxoplasmosis.

Dwg.0/10

L16 ANSWER 18 OF 61 WPIDS (C) 2003 THOMSON DERWENT

AN 2001-591763 [67] WPIDS

DNC C2001-175566

TI New immunostimulatory oligonucleotide, useful as a vaccine **adjuvant**, stimulates proliferation of B lymphocytes.

DC B04 D16

IN BACHY, M; SODOYER, R; TRANNOY, E

PA (AVET) AVENTIS PASTEUR SA; (AVET) AVENTIS PASTEUR

CYC 94

PI FR 2805265 A1 20010824 (200167)* 14p

WO 2001062909 A1 20010830 (200167) FR

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001035616 A 20010903 (200202)
ADT FR 2805265 A1 FR 2000-2057 20000218; WO 2001062909 A1 WO 2001-FR349 20010207; AU 2001035616 A AU 2001-35616 20010207
FDT AU 2001035616 A Based on WO 200162909
PRAI FR 2000-2057 20000218
AB FR 2805265 A UPAB: 20011119
NOVELTY - Immunostimulatory oligonucleotide (I) contains the motif (Ia) provided that (Ia) does not contain the dinucleotide CG where C is unmethylated, is new.

DETAILED DESCRIPTION - Immunostimulatory oligonucleotide (I) contains the motif (Ia) at least once, provided that (Ia) does not contain the dinucleotide CG where C is unmethylated.

5'-GAGAATTCTTTACCT4AT-3' (Ia)

An INDEPENDENT CLAIM is also included for a vaccine composition comprising at least one **antigen** (Ag) and at least one of (I).

ACTIVITY - Immunostimulatory. Human peripheral blood lymphocytes (2.5 million in 0.1 ml) were mixed with 0.1 ml of 0.8 mu M solution of (Ia) and incubated for 3 days at 37 deg. C. Then tritiated thymidine was added, culture continued for 7-8 hr and proliferation assessed from incorporation of radioactivity into the cells. At a final concentration of 0.4 mu M (Ia), the index of stimulation was about 22, and 1 for a negative control.

MECHANISM OF ACTION - None given.

USE - (I) is used in pharmaceuticals, especially as immunostimulants in human medicine, or as vaccine adjuvants or compositions, for therapeutic or prophylactic use, and containing one or more antigens.

Dwg.0/2

L16 ANSWER 19 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-591762 [67] WPIDS
DNC C2001-175565
TI New immunostimulatory oligonucleotide, useful as a vaccine **adjuvant**, stimulates proliferation of B lymphocytes.
DC B04 D16
IN BACHY, M; SODOYER, R; TRANNOY, E
PA (AVET) AVENTIS PASTEUR SA; (AVET) AVENTIS PASTEUR
CYC 94
PI FR 2805264 A1 20010824 (200167)* 14p
WO 2001062910 A1 20010830 (200167) FR
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001035617 A 20010903 (200202)
ADT FR 2805264 A1 FR 2000-2056 20000218; WO 2001062910 A1 WO 2001-FR350 20010207; AU 2001035617 A AU 2001-35617 20010207
FDT AU 2001035617 A Based on WO 200162910
PRAI FR 2000-2056 20000218
AB FR 2805264 A UPAB: 20011119
NOVELTY - Immunostimulatory oligonucleotide (I) comprising the motif (Ia), which occurs at least once, provided that it does not contain the dinucleotide CG where C is unmethylated, is new.

DETAILED DESCRIPTION - Immunostimulatory oligonucleotide comprising the motif (Ia), which occurs at least once, provided that it does not contain the dinucleotide CG where C is unmethylated.

5'-GCATGAT-4GAGCT-3' (Ia)

An INDEPENDENT CLAIM is also included for a vaccine composition comprising at least one **antigen** (Ag) and at least one of (Ia).

ACTIVITY - Immunostimulatory. Human peripheral blood lymphocytes (2.5 million in 0.1 ml) were mixed with 0.1 ml of 4 mu M solution of (Ia) and incubated for 3 days at 37 deg. C. Tritiated thymidine was added, and the mixture was cultured for a further 7-8 hours. Proliferation was assessed by observing incorporation of radioactivity into the cells. At a final concentration of 2 mu M (Ia), the index of stimulation was about 20; compared with a value of 1 for a negative control.

MECHANISM OF ACTION - None given.

USE - (I) is used in pharmaceuticals, especially as immunostimulants in human medicine or as vaccine adjuvants or compositions, for therapeutic or prophylactic use, and containing one or more antigens.

Dwg.0/2

L16 ANSWER 20 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-193144 [20] WPIDS
DNC C2001-058085
TI Use of antigenic proteins, peptides, interferon or their encoding DNA, in the manufacture of an agent for the induction of **antigen** -specific T cells.
DC B04 D16
IN GOTOH, M; TAKASU, H; YAMAOKA, T
PA (SUMU) SUMITOMO PHARM CO LTD; (SUMU) SUMITOMO SEIYAKU KK
CYC 27
PI EP 1074267 A1 20010207 (200120)* EN 25p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2313392 A1 20010122 (200120) EN
JP 2001089389 A 20010403 (200126) 13p
ADT EP 1074267 A1 EP 2000-306263 20000724; CA 2313392 A1 CA 2000-2313392 20000724; JP 2001089389 A JP 2000-217966 20000718
PRAI JP 1999-207687 19990722
AB EP 1074267 A UPAB: 20010611

NOVELTY - Use of interferons (IFNs) or DNAs capable of expressing the interferons and/or antigenic proteins (AP), antigenic peptides derived from the proteins or DNAs capable of expressing the antigenic proteins or peptides, in the manufacture of an agent for induction of **antigen** -specific T cells, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a product containing IFNs (or DNA encoding the IFNs) and/or AP (or DNA capable of expressing AP) for use in the induction of **antigen** -specific T cells.

ACTIVITY - Virucide; cytostatic.

MECHANISM OF ACTION - Gene therapy; inducer of **antigen** -specific T cells. The action of interferon- alpha (IFN- alpha) in a system for inducing specific cytotoxic T cell (CTL) by administering an antigenic peptide in an incomplete Freund's **adjuvant** (IFA) **emulsion** preparation form was evaluated. The peptide Flu(366-374) (a restrictive **antigen** peptide derived from influenza virus, ASNESMETM), IFA and IFN- alpha were prepared with phosphate buffered saline (PBS) and IFA. 0.1 ml of this **emulsion** was subcutaneously administered to the tail base of a C57BL/6 mouse. For each group, three mice were used. After 7 days from the drug administration, splenocytes were prepared and re-stimulation was carried out with the peptide in the same manner. After 5 days of culture, cytotoxic activity was determined by 51Cr release method. The cytotoxic activity for peptide non-pulsed EL-4 (undefined) cells was as low as 10% or less in all groups. More potent cytotoxic activity was induced in the group subjected to administration of the peptide and IFN- alpha than in the group subjected to administration of the peptide alone in the IFA form. These results indicated that IFN-alpha exhibited the action of enhancing induction of peptide specific CTL induction even in the IFA preparation form.

USE - IFNs (or DNA encoding IFNs) are useful in the manufacture of a medicament for inducing **antigen**-specific T cells in an individual whose has been administered with AP (or DNA encoding AP) or vice versa. The medicament is useful for the treatment or prophylaxis of a tumor or a viral infectious disease (claimed).
Dwg.0/2

L16 ANSWER 21 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2001294717 EMBASE
TI Intranasal vaccination against plague, tetanus and diphtheria.
AU Alpar H.O.; Eyles J.E.; Williamson E.D.; Somavarapu S.
CS H.O. Alpar, School of Pharmacy, University of London, 29-39 Brunswick Square, London WC1N 1AX, United Kingdom. oya.alpar@amsl.ulsop.ac.uk
SO Advanced Drug Delivery Reviews, (23 Sep 2001) 51/1-3 (173-201).
Refs: 140
ISSN: 0169-409X CODEN: ADDREP
PUI S 0169-409X(01)00166-1
CY Netherlands
DT Journal; General Review
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Plague is an extremely virulent and potentially lethal infection caused by the bacterium Y. pestis. The current vaccine used to immunise against plague often fails to engender solid (100%) protection against inhalational infection with Y. pestis. Similarly, logistical factors favour the development of non-parenteral immunisation protocols to counter plague. Recently an improved parenteral vaccination strategy for plague, based on the recombinant subunit approach, has entered clinical trails. The Yersinia pestis subunit antigens (F1 and V) have been successfully incorporated into novel vaccine delivery systems such as biodegradable microspheres composed of poly-L-(lactide) (PLLA). Intranasal and intratracheal administration of PLLA microencapsulated F1 and V serves to protect experimental animals from inhalational and subcutaneous challenge with virulent Y. pestis bacilli. **Liposomes** have also been used to improve the immunogenicity of intranasally administered Y. pestis antigens, and the effectiveness of this approach to plague immunisation has been evaluated. Tetanus and diphtheria still cause many deaths worldwide. The maintenance of protective immunity to diphtheria and tetanus requires booster injections of the currently licensed toxoid vaccines. Consequently, many people remain unprotected. Improved coverage may well result from the development of effective non-invasive vaccines that could be readily distributed and potentially self-administered. To this end, the intranasal and inhalational routes of administration have been extensively investigated. Tetanus and diphtheria toxoids have been delivered intranasally to experimental animals using a wide variety of adjuvants (enterotoxin derivatives), penetration enhancers (cyclodextrins, bile salts, surfactants, cationic polymers) and delivery systems (microspheres and **liposomes**). As compared with parenteral vaccination, nasal immunisation has been shown favourably effective in small animal models, and a limited number of early phase clinical trails. As a caveat to this, adjuvantisation of toxoid/subunit molecules appears to be a requisite for elicitation of appreciable immunological responses, following nasal administration of acellular immunogens. Testing in larger animal models and humans is needed to ascertain if the promising results obtained in rodents can be reciprocated without compromising safety.

L16 ANSWER 22 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2001335337 EMBASE

TI Recent developments in adjuvants for vaccines against infectious diseases.
AU O'Hagan D.T.; MacKichan M.L.; Singh M.
CS D.T. O'Hagan, Chiron Corporation, Immunology and Infectious Diseases, 4560 Horton Street, Emeryville, CA 94608, United States.
derek_o'hagan@chiron.com
SO Biomolecular Engineering, (2001) 18/3 (69-85).
Refs: 220
ISSN: 1389-0344 CODEN: BIENFV
PUI S 1389-0344(01)00101-0
CY Netherlands
DT Journal; General Review
FS 006 Internal Medicine
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB New generation vaccines, particularly those based on recombinant proteins and DNA, are likely to be less reactogenic than traditional vaccines, but are also less immunogenic. Therefore, there is an urgent need for the development of new and improved vaccine adjuvants. Adjuvants can be broadly separated into two classes, based on their principal mechanisms of action; vaccine delivery systems and 'immunostimulatory adjuvants'. Vaccine delivery systems are generally particulate e.g. emulsions, microparticles, iscoms and **liposomes**, and mainly function to target associated antigens into **antigen** presenting cells (APC). In contrast, immunostimulatory adjuvants are predominantly derived from pathogens and often represent pathogen associated molecular patterns (PAMP) e.g. LPS, MPL, CpG DNA, which activate cells of the innate immune system. Once activated, cells of innate immunity drive and focus the acquired immune response. In some studies, delivery systems and immunostimulatory agents have been combined to prepare **adjuvant** delivery systems, which are designed for more effective delivery of the immunostimulatory **adjuvant** into APC. Recent progress in innate immunity is beginning to yield insight into the initiation of immune responses and the ways in which immunostimulatory adjuvants may enhance this process. However, a rational approach to the development of new and more effective vaccine adjuvants will require much further work to better define the mechanisms of action of existing adjuvants. The discovery of more potent adjuvants may allow the development of vaccines against infectious agents such as HIV which do not naturally elicit protective immunity. New adjuvants may also allow vaccines to be delivered mucosally. .COPYRGT. 2001 Published by Elsevier Science B.V.

L16 ANSWER 23 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2001428649 EMBASE
TI [Vaccines and vaccine adjuvants].
ASILAR VE ASI ADJUVANLAN.
AU Eratalay A.; Oner F.
CS A. Eratalay, Hacettepe Universitesi, Eczacilik Fakultesi, Farmasotik Biyoteknoloji Anabilim, Ankara, Turkey
SO Fabad Journal of Pharmaceutical Sciences, (2001) 26/1 (21-33).
Refs: 99
ISSN: 1300-4182 CODEN: FBDEDQ
CY Turkey
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LA Turkish

SL English; Turkish
AB New vaccines have some advantages due to their purity and safety characteristics, over conventional vaccines, but preventive properties need to be progressed. This can be achieved by using some materials or carriers called adjuvants which helps to increase immune response to an **antigen**. There are two **adjuvant** formulations which have been used since 1950's. One of them is mineral oil emulsions including micobacteria or not, second one is gel or suspension formulations of aluminium salts. Studies on new adjuvants or **adjuvant** carriers are increasing due to the side effects of conventional adjuvants. Recently new adjuvants and carrier systems for modern vaccines are attracting more attention because of the poor immunogenicity of pure subunit or synthetic recombinant antigens and problems with aluminium based adjuvants. New adjuvants have to be nontoxic, noncarcinogenic, must not cause local and systemic reactions and they have to provide long term immune protection with small number of application. In this article **adjuvant** carrier systems and materials used for subunit and recombinant DNA derived vaccines are reviewed.

L16 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2003 ACS
AN 2002:346583 CAPLUS
DN 138:95279
TI **Liposomes** and emulsions as adjuvants for immunization: Mechanisms for amplification of immune effectors through controlled release
AU Alving, Carl R.; Rao, Mangala; Matyas, Gary R.
CS Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Silver Spring, MD, 20910-7500, USA
SO Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 1, 12-13 Publisher: Controlled Release Society, Minneapolis, Minn. CODEN: 69CNY8
DT Conference; General Review
LA English
AB A review discussing mechanisms of controlled-release of **antigen** for immunization by **antigen**-encapsulated **liposomes** in relation to interaction with **antigen** presenting cell (APC), and utilization of adjuvants contg. **liposome**-stabilized emulsions. In addn. to the class II pathway, the authors have discovered that a large amt. of **liposomal antigen** is also released into the cytoplasm of the APC where it is degraded to lipopeptides and delivered to the Golgi complex. Subsequent studies with **liposome**-stabilized emulsions have demonstrated that this formulation shows considerable promise for creating vaccines against **liposome**-encapsulated viral antigens and tumor antigens.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 25 OF 61 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 6
AN 2000-594516 [56] WPIDS
CR 2000-594515 [56]; 2000-594517 [56]; 2000-679550 [66]; 2001-006956 [01]
DNC C2000-177616
TI Novel immunogenic composition comprising at least 1 polysaccharide **antigen** and at least 1 protein **antigen** from Streptococcus pneumoniae, useful in vaccines for treating pneumonia and otitis media.
DC B04 D16
IN CAPIAU, C; DESCHAMPS, M; DESMONS, P M; LAFERRIERE, C A J; POOLMAN, J; PRIEELS, J; FERRIERE, C A J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 92
PI WO 2000056359 A2 20000928 (200056)* EN 77p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000038136 A 20001009 (200103)
BR 2000009166 A 20011226 (200206)
EP 1162999 A2 20011219 (200206) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CZ 2001003379 A3 20020313 (200223)
KR 2002001785 A 20020109 (200246)
HU 2002000373 B 20020628 (200255)
AU 750762 B 20020725 (200260)
ZA 2001007638 A 20020828 (200264) 97p
JP 2002540074 W 20021126 (200307) 97p
CN 1391481 A 20030115 (200330)

ADT WO 2000056359 A2 WO 2000-EP2467 20000317; AU 2000038136 A AU 2000-38136 20000317; BR 2000009166 A BR 2000-9166 20000317, WO 2000-EP2467 20000317; EP 1162999 A2 EP 2000-916983 20000317, WO 2000-EP2467 20000317; CZ 2001003379 A3 WO 2000-EP2467 20000317, CZ 2001-3379 20000317; KR 2002001785 A WO 2000-EP2467 20000317, KR 2001-711941 20010919; HU 2002000373 B WO 2000-EP2467 20000317, HU 2002-373 20000317; AU 750762 B AU 2000-38136 20000317; ZA 2001007638 A ZA 2001-7638 20010917; JP 2002540074 W JP 2000-606263 20000317, WO 2000-EP2467 20000317; CN 1391481 A CN 2000-807773 20000317

FDT AU 2000038136 A Based on WO 200056359; BR 2000009166 A Based on WO 200056359; EP 1162999 A2 Based on WO 200056359; CZ 2001003379 A3 Based on WO 200056359; KR 2002001785 A Based on WO 200056359; HU 2002000373 B Based on WO 200056359; AU 750762 B Previous Publ. AU 200038136, Based on WO 200056359; JP 2002540074 W Based on WO 200056359

PRAI GB 1999-16677 19990715; GB 1999-6437 19990319; GB 1999-9077 19990420; GB 1999-9466 19990423

AB WO 200056359 A UPAB: 20030513

NOVELTY - Immunogenic composition (I) comprising at least 1 Streptococcus pneumoniae polysaccharide **antigen** and at least 1 S. pneumoniae protein **antigen** or immunologically functional equivalent, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of making an immunogenic composition comprising:

(1) selecting at least 1 pneumococcal polysaccharide **antigen**;

(2) selecting at least 1 pneumococcal protein **antigen**; and

(3) mixing the polysaccharide and protein antigens with a suitable excipient.

ACTIVITY - Antibacterial; antiinflammatory; auditory.

MECHANISM OF ACTION - Vaccine.

Balb/c mice (1 year old) were immunized with 1/10th of the human dose of a pneumococcal-polysaccharide/ protein D conjugate vaccine, or 23-valent plain polysaccharide vaccine. Groups of 20 mice were immunized intramuscularly on days 0 and 21 and test bleeds were obtained on day 35. The sera were enzyme-linked immunosorbant antibody (ELISA) tested for IgG antibodies to the pneumococcal polysaccharides. The results showed that immunization with plain polysaccharides did not produce significant amounts of IgG antibodies. Immunization with conjugate vaccines induced IgG antibody with high seroconversion rates against all serotypes except 23F and 2 doses of vaccine formulated with 3D-MPL induced the highest GMC specific IgG and this was statistically significant for all serotypes except 23F, in which case it had a significantly higher seroconversion rate.

USE - (I) is useful as a vaccine, especially (with a TH1 inducing **adjuvant**) for preventing or ameliorating S. pneumoniae infection

and pneumonia in a patient over 55 years, and/or preventing or ameliorating otitis media in infants (claimed).
Dwg.0/1

L16 ANSWER 26 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-041317 [05] WPIDS
DNC C2001-012042
TI New immunostimulatory oligonucleotides, useful e.g. as adjuvants in vaccines for human use, induce lymphocyte proliferation and cytokine secretion.
DC B04 D16
IN BACHY, M; ROQUES, C; SODOYER, R; TRANNOY, E
PA (INMR) PASTEUR MERIEUX SERUMS & VACCINS SA; (AVET) AVENTIS PASTEUR
CYC 92
PI WO 2000075304 A1 20001214 (200105)* FR 30p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2797263 A1 20010209 (200111)
AU 2000055389 A 20001228 (200119)
EP 1196558 A1 20020417 (200233) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000075304 A1 WO 2000-FR1566 20000608; FR 2797263 A1 FR 1999-10378 19990806; AU 2000055389 A AU 2000-55389 20000608; EP 1196558 A1 EP 2000-940454 20000608, WO 2000-FR1566 20000608
FDT AU 2000055389 A Based on WO 200075304; EP 1196558 A1 Based on WO 200075304
PRAI FR 1999-10378 19990806; FR 1999-7457 19990608
AB WO 200075304 A UPAB: 20010124
NOVELTY - Immunostimulatory oligonucleotides (I), are new.
DETAILED DESCRIPTION - An immunostimulatory oligonucleotide (I) contains at least one sequence 5'-TTN1N2TT-3' (II), where N1 and N2 are A, T, C or G.
(I) do not contain any CG dinucleotides in which C in unmethylated.
An INDEPENDENT CLAIM is also included for a vaccine composition for human use comprising vaccinating **antigen** (Ag) and at least one (I).
ACTIVITY - Immunostimulant.
Peripheral human blood lymphocytes were incubated for 48-72 hours with 2 micro M various oligonucleotides (all intersugar links phosphorothioate), pulsed for 7-8 hours with tritiated thymidine, then the cells were harvested, washed, dried and incorporated radioactivity measured. The most active compounds for inducing proliferation had formula 5'-TTAGTTCTTAGTTN3TTAGTT where N3 is any nucleotide. Results are not included in the specification.
MECHANISM OF ACTION - Vaccine.
USE - (I) are used as human immunostimulants and as adjuvants in therapeutic and prophylactic vaccines for human use. (I) induce proliferation of human lymphocytes, induce secretion of cytokines, especially interleukin-10 or interferon gamma and increase expression of the CD86 activation marker or the CD25 cytokine receptor on human B lymphocytes.
ADVANTAGE - (I) are selected for their ability to stimulate human cells (contrast known methods where selection uses murine cells). Apart for increasing the immune response, (I) may also redirect it, e.g. towards a cellular rather than humoral response, production of particular cytokines or antibody (sub)types, or stimulation of particular cell types.
Dwg.0/0

L16 ANSWER 27 OF 61 WPIDS (C) 2003 THOMSON DERWENT

AN 2000-587476 [55] WPIDS
DNC C2000-175273
TI Use of Klebsiella membrane fraction as **adjuvant**, for e.g. antitumor or antiviral vaccines, to direct a Th1, or mixed, immune response against associated **antigen**.
DC B04 D16
IN BECK, A; BONNEFOY, J; CORVAIA, N; LIBON, C; NGUYEN, T N; N'GUYEN, T N; BONNEFOY, J Y; N GUYEN, T
PA (FABR) FABRE MEDICAMENT SA PIERRE
CYC 27
PI WO 2000054789 A1 20000921 (200055)* FR 35p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CN JP MX US ZA
FR 2790959 A1 20000922 (200055)
AU 2000032980 A 20001004 (200101)
EP 1158993 A1 20011205 (200203) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 2000009051 A 20020102 (200206)
CN 1343124 A 20020403 (200247)
ZA 2001007628 A 20020828 (200264) 66p
JP 2002539169 W 20021119 (200281) 34p
ADT WO 2000054789 A1 WO 2000-FR622 20000315; FR 2790959 A1 FR 1999-3153 19990315; AU 2000032980 A AU 2000-32980 20000315; EP 1158993 A1 EP 2000-910946 20000315, WO 2000-FR622 20000315; BR 2000009051 A BR 2000-9051 20000315, WO 2000-FR622 20000315; CN 1343124 A CN 2000-805044 20000315; ZA 2001007628 A ZA 2001-7628 20010917; JP 2002539169 W JP 2000-604864 20000315, WO 2000-FR622 20000315
FDT AU 2000032980 A Based on WO 200054789; EP 1158993 A1 Based on WO 200054789; BR 2000009051 A Based on WO 200054789; JP 2002539169 W Based on WO 200054789
PRAI FR 1999-3153 19990315
AB WO 200054789 A UPAB: 20021105
NOVELTY - Use of a membrane fraction (A) from Klebsiella pneumoniae, associated with an **antigen** or hapten (I), for preparation of a pharmaceutical composition that directs a Th1, or mixed Th1/Th2 immune response against (I), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising (A) associated with (I).

ACTIVITY - Cytostatic; virucide; antibacterial; antifungal; antiparasitic.

The recombinant protein BBG2Na (comprising the 101 amino acid peptide, G2Na, from the G protein of respiratory syncytial virus (RSV) and the C-terminal fragment of protein G of streptococcus) was used to immunize mice (two 20 micro g subcutaneous injections), in combination with various amount of a membrane fraction (A) from Klebsiella pneumoniae. Blood samples analyzed after 28 days showed a significant increase in IgG response to G2Na, relative to administration of BBG2Na in saline, comparable to that induced by alum or Freund's **adjuvant**. In presence of 0.1 mg (A), titers of IgG1 and IgG2a were roughly the same; contrast alum and Freund's **adjuvant** which strongly favored an IgG1 response. Three weeks after the second immunization, the mice were challenged with 105 TCID50 of type A RSV. Examination of lungs after a further 5 days showed that the animals had been protected against infection.

MECHANISM OF ACTION - Induction of a specific immune response.

USE - The (A)/(I) product is used for treatment or prevention of infectious diseases (viral, bacterial, fungal or parasitic) or cancers, most especially infections by paramyxoviruses, specifically respiratory syncytial virus or parainfluenza.

ADVANTAGE - (A) not only increases the antibody response to (I), but also directs the cytokine response towards a Th1(or mixed, Th1/Th2) type, especially favoring production of Ig2a subtype antibodies.

Dwg.0/4

L16 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2003 ACS
AN 2000:608610 CAPLUS
DN 133:206755
TI Immunogens comprising a peptide and a carrier derived from Haemophilius influenzae protein D
IN Coste, Michel; Lobet, Yves; Van-Mechelen, Marcelle Paulette; Verriest, Christophe
PA Smithkline Beecham Biologicals S.A., Belg.
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000050077	A1	20000831	WO 2000-EP1457	20000222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156825	A2	20011128	EP 2000-909235	20000222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537354	T2	20021105	JP 2000-600687	20000222

PRAI GB 1999-4405 A 19990225
GB 1999-4408 A 19990225
GB 1999-4412 A 19990225
GB 1999-19260 A 19990813
WO 2000-EP1457 W 20000222

AB The present invention provides peptide immunogens linked to a carrier wherein the carrier is derived from Haemophilius Influenzae Protein D or fragments thereof. Compns comprising the **antigen** peptide, protein D epitope or mimotope, and immune **adjuvant** (e.g. saponin, aluminum salt, oil in water **emulsion**, or **liposome**) are useful for treating infection or chronic diseases.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 29 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000094262 EMBASE
TI Delivery systems for molecular vaccination.
AU Sheikh N.A.; Al-Shamisi M.; Morrow W.J.W.
CS N.A. Sheikh, Department of Pharmaceutics, Washington Reg. Primate Res. Center, University of Washington, Seattle, WA 98121, United States
SO Current Opinion in Molecular Therapeutics, (2000) 2/1 (37-54).
Refs: 162
ISSN: 1464-8431 CODEN: CUOTFO
CY United Kingdom
DT Journal; General Review
FS 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LA English
SL English
AB Vaccination is one of the medical success stories of the 20th century, however, there are many diseases for which no prophylactic regimes are available. A major hindrance that has prevented the development of effective mass immunization programs is the inability to induce an

appropriate, protective, immune response. For example, for vaccines against intracellular pathogens there is a requirement for cell-mediated immunity as characterized by cytolytic T-lymphocyte activity. However, such a response can be extremely difficult to elicit, especially those employing recombinant, soluble protein subunits. This deficiency is due to the inability of these antigens to access the machinery of the appropriate **antigen**-processing pathway. Following an improved understanding of the mechanisms underlying such processing, as well as the realization that delivery systems can affect, quantitatively and qualitatively, the resulting immune response, the last decade has witnessed an intense research effort in this field. In this article we will review the major developments in the area of **antigen** delivery as related to vaccination.

L16 ANSWER 30 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
AN 2000:534629 BIOSIS
DN PREV200000534629
TI Induction and detection of antibodies to squalene.
AU Matyas, Gary R. (1); Wassef, Nabila M.; Rao, Mangala; Alving, Carl R.
CS (1) Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Silver Spring, MD, 20910-7500 USA
SO Journal of Immunological Methods, (1 November, 2000) Vol. 245, No. 1-2, pp. 1-14. print.
ISSN: 0022-1759.
DT Article
LA English
SL English
AB An enzyme-linked immunosorbent assay (ELISA) utilizing **antigen** coated on hydrophobic polyvinyldiene fluoride (PVDF) membranes is described for detecting antibodies that bind to squalene (SQE). Because of the prior lack of availability of validated antibodies to SQE, positive controls for the assay were made by immunization with formulations containing SQE to create monoclonal antibodies (mAbs) that reacted with SQE. Among eight immunogens tested, only two induced detectable murine antibodies to SQE: **liposomes** containing dimyristoyl phosphatidylcholine, dimyristoyl phosphatidylglycerol, 71% SQE, and lipid A (L(71% SQE+LA)), and, to a much lesser extent, an oil-in-water **emulsion** containing SQE, Tween 80, Span 85, and lipid A. In each case, lipid A served as an **adjuvant**, but neither SQE alone, SQE mixed with lipid A, **liposomes** containing 43% SQE and lipid A, nor several other emulsions containing both SQE and lipid A, induced antibodies that reacted with SQE. Monoclonal antibodies produced after immunizing mice with (L(71% SQE+LA)) served as positive controls for developing the ELISA. Monoclonal antibodies were produced that either recognized SQE alone but did not recognize squalane (SQA, the hydrogenated form of SQE), or that recognized both SQE and SQA. As found previously with other **liposomal** lipid antigens, **liposomes** containing lipid A also induced antibodies that reacted with the **liposomal** phospholipids. However, mAbs were also identified that reacted with SQE on PVDF membranes, but did not recognize either SQA or **liposomal** phospholipid. The polyclonal antiserum produced by immunizing mice with (L(71% SQE+LA)) therefore contained a mixed population of antibody specificities and, as expected, the ELISA of polyclonal antiserum with PVDF membranes detected antibodies both to SQE and SQA. We conclude that SQE is a weak **antigen**, but that antibodies that specifically bind to SQE can be readily induced by immunization with (L(71% SQE+LA)) and detected by ELISA with PVDF membranes coated with SQE.

L16 ANSWER 31 OF 61 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 8
AN 1999-620288 [53] WPIDS
DNC C1999-181049

TI Enhancing mammalian immune response, useful for treating individuals suffering from an immuno-compromised disease or disorder e.g. AIDS and/or for use with chemotherapy recipients.

DC B04 D16

IN BRENNER, M B; DASCHER, C C; HIROMATSU, K; PORCELLI, S A

PA (BGHM) BRIGHAM & WOMENS HOSPITAL INC; (BGHM) BRIGHAM WOMENS HOSPITAL INC

CYC 86

PI WO 9952547 A1 19991021 (199953)* EN 49p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9935588 A 19991101 (200013)
EP 1071452 A1 20010131 (200108) EN
R: AT BE DE ES FI FR GB IE IT SE
JP 2002511421 W 20020416 (200242) 52p

ADT WO 9952547 A1 WO 1999-US8112 19990413; AU 9935588 A AU 1999-35588 19990413; EP 1071452 A1 EP 1999-917473 19990413, WO 1999-US8112 19990413; JP 2002511421 W WO 1999-US8112 19990413, JP 2000-543157 19990413

FDT AU 9935588 A Based on WO 9952547; EP 1071452 A1 Based on WO 9952547; JP 2002511421 W Based on WO 9952547

PRAI US 1998-81638P 19980413

AB WO 9952547 A UPAB: 20011203
NOVELTY - A method of enhancing an immune response in a mammal to at least one CD1 **antigen** is new and comprises co-administering to the mammal an effective amount of at least one CD1 **antigen** and at least one T cell stimulating compound.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of vaccinating a mammal against at least one CD1 **antigen** comprising administering to the mammal an effective amount of at least one CD1 **antigen** and at least one **adjuvant**;

(2) a method of stimulating a CD1-restricted immune response in a mammal comprising administering to the mammal a composition comprising at least one **adjuvant** and at least one lipid **antigen** where the **antigen** elicits a CD1-restricted immune response;

(3) an immunogenic composition (I), comprising:

(a) at least one T cell stimulating compound; and

(b) at least one CD1 **antigen**, where the CD1 **antigen** elicits a CD1-restricted immune response;

(4) a method for eliciting an immunogenic response in a mammal comprising administering (I);

(5) a vaccine composition (II) comprising at least one **adjuvant** and at least one lipid **antigen** where the lipid **antigen** elicits a CD1-restricted immune response;

(6) a method for vaccinating a mammal comprising administering (II); and

(7) a kit comprising at least one T-cell stimulating compound and at least one CD1 **antigen** where the CD1 **antigen** elicits a CD1-restricted immune response.

ACTIVITY - Anti-parasitic; antibacterial; immune stimulant.

MECHANISM OF ACTION - The method elicits at least one immunological parameter e.g. antibody response the **antigen**, cytotoxic T-lymphocyte response, T-cell proliferation, helper T-cell response or a T-cell modulated cytokine response.

USE - The method is useful for enhancing or boosting the immune response of an individual who has a immuno-compromised disease, disorder or condition (e.g. AIDS or chemotherapy recipient). The method is also useful for eliciting or boosting an immune response for at least one bacterial infection (e.g. Mycobacteria genus, Hemophilus genus, Streptococcus genus, Staphylococcus genus and Chlamydia) and/or at least

one parasitic infection (e.g. Plasmodium or Trypanosoma genus). (All claimed). The CD1 **antigen** can also be a tumor associated or derived **antigen** that is involved in diseases e.g. cancer (e.g. melanoma, breast cancer, prostate cancer, and colo-rectal cancer) or a self **antigen** that is involved in autoimmune diseases (e.g. diabetes, Lupus, rheumatoid arthritis).

ADVANTAGE - The method enhances the immune response for vaccines without eliciting a sufficient protective immune response in a host.

Dwg.0/7

L16 ANSWER 32 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-106101 [09] WPIDS
DNN N2000-081471 DNC C2000-031931
TI Method for production of toxoplasma **antigen** SAG1 for use in vaccines.
DC B04 D16 S03
IN BIEMANS, R; BOLLEN, A; HAUMONT, M
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 87
PI WO 9966043 A1 19991223 (200009)* EN 47p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9945102 A 20000105 (200024)
EP 1086228 A1 20010328 (200118) EN
R: BE CH DE ES FR GB IT LI NL
ADT WO 9966043 A1 WO 1999-EP3957 19990608; AU 9945102 A AU 1999-45102 19990608; EP 1086228 A1 EP 1999-927922 19990608, WO 1999-EP3957 19990608
FDT AU 9945102 A Based on WO 9966043; EP 1086228 A1 Based on WO 9966043
PRAI GB 1999-8564 19990415; GB 1998-12773 19980612
AB WO 9966043 A UPAB: 20000218

NOVELTY - A novel method for the production of the toxoplasma **antigen** SAG1 or a fragment of it, comprises constructing a plasmid comprising DNA encoding SAG1 or a fragment of it, transforming a P. pastoris host cell with the plasmid, and culturing the host cell such that the DNA encoding SAG1 or a fragment of it is expressed.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) the plasmid pNIV3488;

(2) a SAG1 protein or fragment expressed in P. pastoris;

(3) a vaccine composition comprising the protein of (2) in combination with a suitable **adjuvant** and/or carrier;

(4) a truncated SAG1 protein in which the anchor region of SAG1 is absent;

(5) a vaccine composition comprising the protein of (4) in combination with a suitable **adjuvant** and/or carrier;

(6) use of the protein of (2) or (4) in the manufacture of a medicament for the prevention or treatment of toxoplasmosis infections in mammals; and

(7) a diagnostic kit for the diagnosis of toxoplasmosis infection in the blood of mammals which may be infected, the kit comprises an anchor-less SAG1 **antigen** or a fragment of it.

ACTIVITY - Protozoacide.

MECHANISM OF ACTION - Vaccine.

USE - The SAG1 protein, fragment, and truncated variant can be used in the manufacture of a medicament for the prevention or treatment of toxoplasmosis in mammals (claimed).

ADVANTAGE - None given.

Dwg.0/0

L16 ANSWER 33 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-105687 [09] WPIDS
DNC C2000-031718
TI Novel immunomodulatory oligonucleotide used to induce a Th1-type immune response, e.g. to tumor antigens.
DC B04 D16
IN SCHWARTZ, D
PA (DYNA-N) DYNAVAX TECHNOLOGIES CORP
CYC 86
PI WO 9962923 A2 19991209 (200009)* EN 52p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9944194 A 19991220 (200021)
EP 1121373 A2 20010808 (200146) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6562798 B1 20030513 (200335)
AU 760304 B 20030515 (200337)
ADT WO 9962923 A2 WO 1999-US12538 19990604; AU 9944194 A AU 1999-44194 19990604; EP 1121373 A2 EP 1999-927241 19990604, WO 1999-US12538 19990604; US 6562798 B1 Provisional US 1998-88310P 19980605, US 1999-324191 19990601; AU 760304 B AU 1999-44194 19990604
FDT AU 9944194 A Based on WO 9962923; EP 1121373 A2 Based on WO 9962923; AU 760304 B Previous Publ. AU 9944194, Based on WO 9962923
PRAI US 1999-324191 19990601; US 1998-88310P 19980605
AB WO 9962923 A UPAB: 20000218
NOVELTY - Immunomodulatory oligonucleotide (I) containing an immunostimulatory sequence (ISS) that contains a modified cytosine (mC), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an immunomodulatory oligonucleotide comprising a sequence selected from TGACTGTGAA NGTTCCAGAT GA, TGACGTGGAA NGTTNGAGAT GA, and TGACTGTGAA NGTTCGAGAT GA;

(2) composition containing (I) and an **antigen** (Ag), optionally also an **adjuvant**;

(3) a composition containing (I) and a facilitator (II), i.e. a co-stimulatory molecule, cytokine, chemokine, targeting protein ligand, transactivating factor or peptide (optionally containing a modified amino acid); and

(4) a method for modulating an immune response by administering compositions of (2) or (3).

ACTIVITY - Immunomodulatory; antitumor; anti-allergic; anti-asthma; antiviral; antibacterial; antiprotozoal; antifungal; contraceptive.

MECHANISM OF ACTION - (I) have an **adjuvant**-like effect and stimulate production of Th1-type cytokines. Human peripheral blood mononuclear cells were incubated for 1-3 days with the phosphorothioate oligonucleotide tgactgtgAABGTTCGagatga (upper case indicates the ISS; B = 5'-bromocytidine) then analyzed for incorporation of tritiated thymidine and secretion of interleukins 6 and 12. This oligonucleotide stimulated proliferation and induced secretion of both cytokines, about as effectively as the analogous compound with B replaced by unmodified C. Similar oligonucleotides that lacked an ISS had no stimulatory effect.

USE - (I) are used, particularly when formulated with an **antigen** (Ag) or a facilitator, for modulating immune responses, particularly for use in tumor therapy; treatment of allergy (including asthma) and for inducing a vigorous cellular response (against a virus, bacterium, fungus or protozoan), also in contraceptive vaccines based on sperm antigens.

ADVANTAGE - When formulated with an **antigen**, (I) induce a

Th1-type immune response, i.e. activation of cytotoxic T cells, particularly effective for control of viruses and intracellular parasites, while simultaneously downregulating the Th2-type response.
Dwg.0/4

L16 ANSWER 34 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-072546 [06] WPIDS
DNC C2000-020733
TI New polypeptides, useful to produce vaccines for neosporosis in animals, especially livestock.
DC B04 C06 D16
IN ATKINSON, R; ELLIS, J T; RYCE, C
PA (INSE-N) INSEARCH LTD
CYC 25
PI WO 9961046 A1 19991202 (200006)* EN 60p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA NO NZ US
AU 9941229 A 19991213 (200020)
EP 1085898 A1 20010328 (200118) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
AU 735498 B 20010712 (200147)
ADT WO 9961046 A1 WO 1999-AU405 19990526; AU 9941229 A AU 1999-41229 19990526; EP 1085898 A1 EP 1999-924579 19990526, WO 1999-AU405 19990526; AU 735498 B AU 1999-41229 19990526
FDT AU 9941229 A Based on WO 9961046; EP 1085898 A1 Based on WO 9961046; AU 735498 B Previous Publ. AU 9941229, Based on WO 9961046
PRAI AU 1998-3717 19980526
AB WO 9961046 A UPAB: 20000203
NOVELTY - An isolated polypeptide (I) forming a Neospora caninum **antigen** is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) An isolated nucleic acid molecule (II) encoding (I) comprising:
(a) a 636 (A) or a 1712 bp (B) sequence as given in the specification;
(b) functional equivalents or portions of (A) or (B);
(c) sequences which hybridize to (A) or (B); or
(d) sequences which have at least 60% homology with (A) or (B).
(2) A vector (III) comprising (II);
(3) A composition (IV) comprising (I), mixtures of or immunogenic fragments of (I); and
(4) A composition (V) comprising (III) and a carrier.
ACTIVITY - Anti-protozoal.
MECHANISM OF ACTION - Vaccine.
USE - The polypeptides and vectors are useful in obtaining a protective effect against neosporosis in animals (claimed). (IV) (especially comprising sequence D) and (V) (especially when the plasmid is VR1012 and includes sequence A or B) can be used to raise an immune response against neosporosis in animals (claimed), i.e. in vaccines to protect animals against neosporosis. The polypeptides (especially NcGra2) are also useful to detect antibodies reactive or specific to Neospora (claimed) e.g. to screen herds for infected animals or to determine the effectiveness of immunization. The polypeptides may be used to produce antibodies, also useful in assays to detect N. caninum to protect against neosporosis.
ADVANTAGE - The polypeptides allow for development of vaccines for neosporosis, which may be practical for controlling the disease in cattle, unlike current chemical treatment.
Dwg.0/8

L16 ANSWER 35 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9
AN 1999:242627 BIOSIS
DN PREV199900242627

TI Biodegradable microspheres containing influenza A vaccine: Immune response in mice.
AU Hilbert, Anne K.; Fritzsche, Ulrike; Kissel, Thomas (1)
CS (1) Department of Pharmaceutics and Biopharmacy, Philipps-University, D-35032, Marburg Germany
SO Vaccine, (March, 1999) Vol. 17, No. 9-10, pp. 1065-1073.
ISSN: 0264-410X.
DT Article
LA English
SL English
AB A monovalent influenza split vaccine was microencapsulated in poly(D,L-lactic-co-glycolic acid) (PLGA) and ABA triblock copolymers using a W/O/W double **emulsion** technique. To stabilize the **antigen**, influenza vaccine was also coencapsulated with **liposomes**. **Antigen** release from microspheres was determined in vitro using a hemagglutinin-specific ELISA. PLGA-microspheres with **liposomes** released immunoreactive hemagglutinin in a pulsatile manner, a preferred feature for the development of a single dose vaccine delivery system. Influenza hemagglutinin specific IgG and neutralizing antibody responses were studied in BALB/c mice following subcutaneous injection of different microsphere preparations. PLGA-microspheres elicited a significantly higher primary IgG response compared to nonencapsulated **antigen**. ABA-microspheres seemed to be less immunogenic than PLGA-microspheres based on the IgG antibody response, however, similar levels of neutralizing antibodies were observed after eight weeks with both polymers. Entrapment of the **antigen** in **liposomes** prior to microencapsulation did not further enhance the immune response. The immunopotentating effect of the **antigen**-loaded microspheres was prominently enhanced when they were given as suspension in fluid **antigen**, suggesting that free **antigen** may serve as priming and microencapsulated **antigen** as booster dose. Eight weeks after a single subcutaneous immunization with PLGA or ABA-microspheres neutralizing antibodies were as high as those obtained after two subcutaneous administrations of fluid vaccine four weeks apart. Microencapsulated influenza **antigen** may have potential for a single dose vaccine delivery system with **adjuvant** properties.

L16 ANSWER 36 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1999083467 EMBASE
TI Mucosal vaccine delivery.
SO Expert Opinion on Therapeutic Patents, (1999) 9/3 (255-262).
Refs: 33
ISSN: 1354-3776 CODEN: EOTPEG
CY United Kingdom
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Vaccine development and vaccination is a major growth area of the pharmaceutical industry. As new vaccine products become available, potential will be given to physicians to provide prophylaxis for diseases that were previously not preventable, or to improve immunisation for some diseases that are currently suboptimally covered. Many factors influence vaccine effectiveness but one of the most important is the route of delivery of the product. Mucosal delivery of vaccines allows primary immunisation at the sites of the body where many of mankind's mortality- and morbidity-causing diseases are initiated. Effective mucosal immunity is best induced by mucosal delivery of vaccines, due to the specialised and interlinked nature of the mucosal lymphoid tissues. As well as the potential for enhanced immunity, mucosal vaccine delivery is expected to

increase patient compliance, make vaccines easier to use and reduce the pain, side-effects and fear of parenteral injection. However, mucosal delivery of vaccines is not straightforward and several strategies have been developed to allow for administration by the oral, nasal, rectal, genito-urinary and even pulmonary routes. These strategies include the use of live attenuated micro-organisms, attenuated toxins, bioadhesive polymers and emulsions, **liposomes** and proteosomes, biodegradable microparticles and immune stimulatory complexes (ISCOMS) as mucosal vaccine delivery systems/adjuvants. Details of some of the recent advances utilising these systems for mucosal **antigen** delivery are included in the article with a brief discussion on some of the strengths and weaknesses of the various strategies.

L16 ANSWER 37 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1999410119 EMBASE
TI **Liposomes** and emulsions as carriers of vaccines.
AU Alving C.R.; Matyas G.R.; Muderhwa J.M.; Spitler L.E.
CS C.R. Alving, Department of Membrane Biochemistry, Walter Reed Army Institute Research, Washington, DC 20307-5100, United States
SO Proceedings of the Controlled Release Society, (1999) -/26 (85-86).
Refs: 15
ISSN: 1022-0178 CODEN: 58GMAH
CY United States
DT Journal; Conference Article
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
038 Adverse Reactions Titles
LA English

L16 ANSWER 38 OF 61 CAPLUS COPYRIGHT 2003 ACS
AN 1998:799982 CAPLUS
DN 130:43356
TI Immunogenic oil-in-water emulsions for use as antitumor adjuvants and in vaccines
IN Alving, Carl R.; Muderhwa, Jean M.; Spitler, Lynn E.
PA Jenner Biotherapies, Inc., USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9853799	A2	19981203	WO 1998-US10806	19980528
	WO 9853799	A3	19990415		

W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	AU 9880538	A1	19981230	AU 1998-80538	19980528
	US 6110492	A	20000829	US 1998-86552	19980528
PRAI	US 1997-47964P	P	19970528		
	WO 1998-US10806	W	19980528		

AB A compn. which comprises a stable oil-in-water **emulsion** having a continuous water phase and a discontinuous oil phase and contg., as sole stabilizing agent, a sufficient quantity of smectic mesophase vesicles and their disintegrated forms to provide at least about 100 mM amphiphile is stable and useful as an **adjuvant**, in a vaccine, or drug delivery system. Data are presented on the use of such **emulsion** with

prostate-specific **antigen** in the treatment of prostate cancer in humans.

L16 ANSWER 39 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1998074807 EMBASE
TI Recent advances in immunological adjuvants: The development of particulate **antigen** delivery systems.
AU O'Hagan D.T.
CS D.T. O'Hagan, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94704, United States
SO Expert Opinion on Investigational Drugs, (1998) 7/3 (349-359).
Refs: 70
ISSN: 1354-3784 CODEN: EOIDER
CY United Kingdom
DT Journal; General Review
FS 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB New generation vaccines, including those based on recombinant proteins, are safer than traditional vaccines, but are less immunogenic. Therefore, there is an urgent need for the development of new and improved vaccine adjuvants. A number of potent immunostimulatory molecules obtained from bacterial cells or plants have been extensively evaluated as adjuvants. However, a number of these molecules have displayed significant toxicity, both in preclinical animal models and in human clinical trials. An alternative approach to the development of novel adjuvants involves the preparation of particulate **antigen** delivery systems of similar dimensions to natural pathogens. In the absence of additional immunostimulatory molecules, **emulsion** droplets and microparticles have been shown to be potent adjuvants for the induction of both humoral and cell-mediated immune responses following systemic administration. Moreover, particulate delivery systems have been shown to display an acceptable toxicity profile in a number of clinical trials. Particulate **antigen** delivery systems also have the potential to function as potent adjuvants following administration by mucosal routes, including oral and intranasal. An alternative approach to the mucosal delivery of vaccines involves the use of genetically detoxified mutant toxins, e.g., LT-K63, as mucosal adjuvants. The use of novel adjuvants and **antigen** delivery systems is likely to extend the use of vaccines into the area of therapeutics, involving the eradication of infectious diseases and cancers, or the amelioration of autoimmune disorders.

L16 ANSWER 40 OF 61 LIFESCI COPYRIGHT 2003 CSA
AN 1999:44892 LIFESCI
TI Vaccine compositions containing **liposomes**
AU Barchfeld, G.L.; Ott, G.; Van Nest, G.A.
CS Chiron Corporation
SO (19980120) . US Patent 5709879; US Class: 424/450; 424/184.1; 424/204.1; 424/234.1; 424/812; 514/2; 514/937; 514/938..
DT Patent
FS W3
LA English
SL English
AB A vaccine composition, comprising an antigenic substance in association with a **liposome** and an oil-in-water **emulsion** comprising a muramyl peptide, a metabolizable oil, and optionally an additional emulsifying agent. The two components of the **adjuvant** (i.e., the **liposome/antigen** component and the **emulsion** component) act together to produce high levels of immune

response.

L16 ANSWER 41 OF 61 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 10
AN 1997-526204 [48] WPIDS
CR 1999-244669 [21]
DNC C1997-167360
TI Vaccine for enhancing T cell response containing **antigen** and **adjuvant** acting via the CD28 receptor - also the new adjuvants and DNA encoding them or T cell dependent antigens.
DC B04 D16
IN HEATH, A W
PA (UYSH-N) UNIV SHEFFIELD; (HEAT-I) HEATH A W
CYC 77
PI WO 9738711 A2 19971023 (199748)* EN 31p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9723031 A 19971107 (199809)
WO 9738711 A3 19971120 (199816)
EP 909179 A2 19990421 (199920) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2002098184 A1 20020725 (200254)
ADT WO 9738711 A2 WO 1997-GB971 19970408; AU 9723031 A AU 1997-23031 19970408; WO 9738711 A3 WO 1997-GB971 19970408; EP 909179 A2 EP 1997-915616 19970408, WO 1997-GB971 19970408; US 2002098184 A1 Cont of US 1998-171063 19981009, US 2002-72583 20020208
FDT AU 9723031 A Based on WO 9738711; EP 909179 A2 Based on WO 9738711
PRAI GB 1996-7711 19960413
AB WO 9738711 A UPAB: 20020823
Vaccine for enhancing T-cell dependent immunity comprises a T-cell dependent **antigen** (Ag), or part of it, and an **adjuvant** (II) that stimulates T cells through the CD28 surface receptor. Also claimed are: (1) a (II) containing an agent that stimulates CD28; (2) a system for producing the vaccine comprising a cell that expresses (part of) Ag and (II), and (3) an isolated DNA encoding one or both of Ag and (II).

Ag is a soluble protein and (II) is able to bind to CD28. Ag and (II) may be crosslinked or present together but not physically joined. (II) is particularly (i) (part of) an antibody that binds CD28, specifically a humanised monoclonal antibody or (ii) based on the natural ligands of CD28 (i.e. proteins B7.1 and B7.2 or their binding fragments). Preferably (II) is a recombinant protein and Ag and (II) comprise a single fusion protein. The vaccine is formulated as an immunostimulatory composition that elicits an enhanced cytotoxic T cell response, e.g. as **liposomes**, biodegradable microspheres or an **emulsion** of Ag and (II) in oil. In the system of (2), the cells secrete Ag and/or (II), either separately or as a fusion protein.

USE - The vaccines may be contraceptive, immunotherapeutic, prophylactic or therapeutic.

ADVANTAGE - Since CD28 is constitutively expressed, timing of vaccination is not critical and (II) is safe to use for increasing immune response to soluble protein Ag.

Dwg.1/8

L16 ANSWER 42 OF 61 WPIDS (C) 2003 THOMSON DERWENT
AN 1997-415074 [38] WPIDS
DNC C1997-132854
TI Composition for treatment and prevention of chicken pox and shingles - contains Varicella zoster virus IE63 protein or nucleic acid encoding it.
DC B04 D16
IN RENTIER, B; SADZOT, C

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (UYLI-N) UNIV LIEGE
CYC 77
PI WO 9728820 A1 19970814 (199738)* EN 28p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9716012 A 19970828 (199750)
ZA 9700971 A 19980527 (199827) 26p
NO 9803617 A 19981002 (199849)
EP 879060 A1 19981125 (199851) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
CZ 9802486 A3 19981216 (199904)
CN 1210470 A 19990310 (199929)
NZ 331164 A 20000228 (200017)
BR 9707400 A 20000104 (200019)
AU 723555 B 20000831 (200046)
KR 99082360 A 19991125 (200055)
MX 9806411 A1 19990601 (200058)
HU 2000001991 A2 20001030 (200064)
US 2001041183 A1 20011115 (200172)
JP 2002504080 W 20020205 (200212) 29p
IL 125440 A 20020210 (200230)
CZ 289971 B6 20020515 (200241)
ADT WO 9728820 A1 WO 1997-EP520 19970204; AU 9716012 A AU 1997-16012 19970204; ZA 9700971 A ZA 1997-971 19970206; NO 9803617 A WO 1997-EP520 19970204, NO 1998-3617 19980806; EP 879060 A1 EP 1997-902334 19970204, WO 1997-EP520 19970204; CZ 9802486 A3 WO 1997-EP520 19970204, CZ 1998-2486 19970204; CN 1210470 A CN 1997-192099 19970204; NZ 331164 A NZ 1997-331164 19970204, WO 1997-EP520 19970204; BR 9707400 A BR 1997-7400 19970204, WO 1997-EP520 19970204; AU 723555 B AU 1997-16012 19970204; KR 99082360 A WO 1997-EP520 19970204, KR 1998-706090 19980807; MX 9806411 A1 MX 1998-6411 19980807; HU 2000001991 A2 WO 1997-EP520 19970204, HU 2000-1991 19970204; US 2001041183 A1 Div ex WO 1997-EP520 19970204, Div ex US 1998-117711 19981020, US 2001-865637 20010525; JP 2002504080 W JP 1997-528141 19970204, WO 1997-EP520 19970204; IL 125440 A IL 1997-125440 19970204; CZ 289971 B6 WO 1997-EP520 19970204, CZ 1998-2486 19970204
FDT AU 9716012 A Based on WO 9728820; EP 879060 A1 Based on WO 9728820; CZ 9802486 A3 Based on WO 9728820; NZ 331164 A Based on WO 9728820; BR 9707400 A Based on WO 9728820; AU 723555 B Previous Publ. AU 9716012, Based on WO 9728820; KR 99082360 A Based on WO 9728820; HU 2000001991 A2 Based on WO 9728820; JP 2002504080 W Based on WO 9728820; IL 125440 A Based on WO 9728820; CZ 289971 B6 Previous Publ. CZ 9802486, Based on WO 9728820
PRAI GB 1996-26882 19961224; GB 1996-2617 19960209
AB WO 9728820 A UPAB: 19970922
A pharmaceutical composition comprises: (1) Varicella zoster virus IE63 protein (P), or its immunologically functional derivatives, and an excipient, or (2) nucleic acid (I) encoding IE63 or its derivatives. Also claimed is (P) for use in medicine and the method of preparing the compositions above.

The compositions may also include another varicella protein, e.g. gp I-V; IE62 or their derivatives, and an **adjuvant**, particularly one that induces a Th1 type response. The preferred **adjuvant** is a water-in-oil **emulsion** containing QS21 and 3D-MPL (3-deacylated monophosphoryl lipid A) with QS21:3D-MPL ratio 1:10-10:1 (preferably 1:1-2.5). The **emulsion** comprises particularly 2-10% squalene; 2-10% alpha -tocopherol and 0.3-3% 'Tween 80'. IE63 may alternatively be encapsulated in a **liposome** or conjugated to an immunostimulatory macromolecule, e.g. killed Bordetella cells or tetanus toxoid. A preferred second **antigen** is gpI in secreted form, optionally combined with IE63 in a fusion protein. The composition is prepared by mixing (P) or (I)

with an **adjuvant**.

USE - (P) is used to manufacture a medicament for prevention or amelioration of Varicella or Zoster. The compositions are used as vaccines to prevent or treat chicken pox or shingles. Typical doses of (P) are 1-1000 (preferably 4-40) mu g, optionally followed by booster doses. (I) can be injected as plasmid DNA directly into muscle or delivered in viral or other vectors, e.g. at 0.05-50 (preferably 0.1-10) mg/kg.

ADVANTAGE - IE63 is expressed during the latency period in the human nervous system, and is a major target of the T cell response which is activated as soon as signs of reactivation of latent virus (development of shingles) appear.

Dwg.2/4

L16 ANSWER 43 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 11

AN 1997:180875 BIOSIS

DN PREV199799472588

TI Increased **adjuvant** efficacy in stimulation of antibody responses after macrophage elimination in vivo.

AU Leenaars, P. P. A. M. (1); Savelkoul, H. F. J.; Hendriksen, C. F. M.; Van Rooijen, N.; Claassen, E.

CS (1) TNO Prevention Health, Div. I and I, P.O. Box 2215, 2301 CE Leiden Netherlands

SO Immunology, (1997) Vol. 90, No. 3, pp. 337-343.
ISSN: 0019-2805.

DT Article

LA English

AB To investigate whether macrophages influence the efficacy of adjuvants, we locally eliminated lymph node macrophages with dichloromethylene diphosphonate containing-**liposomes** before primary immunization. After macrophage elimination, animals were immunized with a soluble **antigen** (TNP-KLH; 2,4,6-trinitrophenyl-keyhole limpet haemocyanin) either in phosphate-buffered saline (PBS), in complete Freund's **adjuvant** (CFA), or in Specol. Specol is a water-in-oil **emulsion**, considered to be less aggressive than CFA, but equally effective. A secondary immunization followed with TNP-KLH. In vivo macrophage elimination before Specol/TNP-KLH immunization resulted in increased **adjuvant** efficacy as measured by (primary) antibody responses. This suggests that the activity of Specol is not primarily mediated through macrophages but rather through other **antigen** -presenting cell types (e.g. dendritic cells, B cells, fibroblasts). The overall quality of produced antibodies, in terms of isotype distribution and affinity maturation, remained the same. After primary injection, CFA/TNP-KLH immunization resulted in significantly higher antibody responses in macrophage-depleted animals and antibody responses did not increase significantly after secondary immunization. However, a booster effect was found when macrophages were not eliminated before CFA/TNP-KLH immunization, suggesting that the presence of macrophages during the first weeks of the primary immune response is essential for the induction of an effective secondary response in CFA immunizations. In conclusion, macrophage depletion before immunization with a soluble T-cell-dependent **antigen** combined with Specol may enhance specific antibody responses without changing the isotype or affinity of the antibodies.

L16 ANSWER 44 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 96280436 EMBASE

DN 1996280436

TI Immunological adjuvants: Mechanisms of action and clinical applications.

AU Sheikh N.; Rajananthanan P.; Morrow W.J.W.

CS Department of Immunology, St Bartholomew's/Royal London, School of Medicine/Dentistry, 38 Little Britain,London EC1A 7BE, United Kingdom

SO Expert Opinion on Investigational Drugs, (1996) 5/9 (1079-1099).
ISSN: 1354-3784 CODEN: EOIDER

CY United Kingdom
DT Journal; General Review
FS 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Adjuvants are a neglected aspect of vaccine formulations, prudent choice of which can enhance the immune response both quantitatively and qualitatively. This review details the evolution and current range of adjuvants, particularly those in clinical trials. The components of different adjuvants are outlined and the manner in which they are thought to work is discussed. **Antigen** processing is an essential requirement of any immune response and these mechanisms are discussed in the context of **adjuvant** action.

L16 ANSWER 45 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 12
AN 1995:21188 BIOSIS
DN PREV199598035488
TI Lipophilic multiple **antigen** peptide system for peptide immunogen and synthetic vaccine.
AU Huang, Wolin; Nardelli, Bernardetta; Tam, James P. (1)
CS (1) Dep. Microbiol. Immunol., Vanderbilt Univ., A 5119 Med. Cent. North, Nashville, TN 37232-2363 USA
SO Molecular Immunology, (1994) Vol. 31, No. 15, pp. 1191-1199. ISSN: 0161-5890.
DT Article
LA English
AB We describe the development and structural requirements of a new lipophilic multiple **antigen** peptide (lipoMAP) system for immunogens that contains a built-in lipophilic **adjuvant** and has the ability to elicit cytotoxic T-lymphocytes (CTLs). In addition to the peptide antigens of choice at the amino terminus, the basic lipoMAP design consists of three components: a tetravalent symmetrical core matrix containing two levels of branching beta-alanyl-lysine as a building unit, a hydrophilic Ser-Ser dipeptide linker, and at the carboxyl terminus, palmitoyl lysines (PL) with alternating chirality. An 18-residue peptide from the third variable region in the gp120 of HIV-1 was used as **antigen** in eight models for a structure-function study. Alternating palmitoyl lysine (PL) was introduced as the lipid anchor and built-in **adjuvant** because D and L Lys (Pal) was found via molecular modeling to best mimic phosphatidylcholine and thus provide the most stable peptide antigens on the ordered lipid membranes. The requirements of the palmitoyl lysines and the L-Ser-L-Ser linker were crucial, since replacement with palmitoyl serines or L-Ser-D-Ser linkers led to a marked decrease in immune response. The stoichiometric ratio of PL vs MAP was also important. Multiple **antigen** peptide (MAP) constructs without the lipophilic PLs, those that were underlipidated and contained one PL, or those that were overlipidated containing four PLs, were ineffective. LipoMAPS containing three palmitic acids elicited significant humoral responses in oil-based **emulsion** and **liposomes**, but not in water or alum formulations. LipoMAP containing only two PLs was found best to be incorporated in **liposomes** and elicited a significant immune response and cytotoxic T-lymphocytes (CTLs). These models were compared favorably with a preparation using tripalmitoyl-S-glyceryl cysteine (P3C) as the lipid anchor. We also developed a modular synthesis of MAP-P3C that incorporated P3C as a premade unit containing a thiopyridine, which simplified the overall scheme and minimized oxidation during stepwise peptide synthesis. This lipoMAP model is a new addition to the design of our macromolecular assemblage approach mimicking peptide antigens on the surface of

micro-organisms. It may be a potentially useful approach to the design of a synthetic vaccine for humans.

L16 ANSWER 46 OF 61 CABA COPYRIGHT 2003 CABI
AN 95:201341 CABA
DN 952216237
TI Enhancement of antibody response of chickens to Salmonella enteritidis vaccines by positively charged **liposomal adjuvant**
AU Hussain, I.
CS Department of PathoBiology, University of Minnesota, St. Paul, MN 55108, USA.
SO Pakistan Veterinary Journal, (1994) Vol. 14, No. 4, pp. 180-184. 16 ref. ISSN: 0253-8318
DT Journal
LA English
AB S. enteritidis killed vaccine and subunit outer membrane proteins (OMP) antigens mixed with positively or negatively charged **liposomes** and in oil-**emulsion** were subcutaneously administered to Leghorn chickens at 6- and 10-weeks of age. **Liposomal** vaccines induced a significantly higher antibody response than did the oil-**emulsion** vaccine. Positively charged **liposomal** vaccines produced a significantly higher. Antibody response then negatively charged as well as oil-**emulsion** adjuvants. The antibody response to OMP and vaccine was not different. The results suggest that the positively charged **liposome** plays a significant role as an **adjuvant** to the enteritidis **antigen**.

L16 ANSWER 47 OF 61 MEDLINE DUPLICATE 13
AN 94209040 MEDLINE
DN 94209040 PubMed ID: 8157443
TI Adjuvants and immune enhancement.
AU Allison A C
SO INTERNATIONAL JOURNAL OF TECHNOLOGY ASSESSMENT IN HEALTH CARE, (1994 Winter) 10 (1) 107-20. Ref: 66
Journal code: 8508113. ISSN: 0266-4623.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199405
ED Entered STN: 19940526
Last Updated on STN: 19940526
Entered Medline: 19940516
AB Adjuvants increase cell-mediated and humoral immune responses to specific antigens. Used with recombinant viral antigens, they can elicit the production of T lymphocytes that lyse target cells, expressing the **antigen** in a genetically restricted fashion. Adjuvants can augment the production of interferon-gamma, thereby favoring the production of protective antibody isotopes, such as immunoglobulin G2a in the mouse. Modern adjuvants display the efficacy of Freund's complete **adjuvant** without its side effects. One such **adjuvant** is Syntex **adjuvant** formulation, a synthetic analogue of muramyl dipeptide in a microfluidized squalane/squalene-in-water **emulsion**. Monophosphoryl lipid A in a similar lipid **emulsion** is also effective. Immune-stimulating complexes of saponin and antigens elicit potent cell-mediated and humoral responses. A purified saponin component has **adjuvant** activity with reduced side effects; **liposomes** also can have **adjuvant** activity.
Administering antigens in adjuvants can overcome low responsiveness in very young and old experimental animals and in those that are genetically low responders. Adjuvants are likely components of a new generation of

recombinant and subunit vaccines.

L16 ANSWER 48 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 94369185 EMBASE
DN 1994369185
TI Mechanisms of action of nonionic block copolymer adjuvants.
AU Hunter R.L.; McNicholl J.; Lal A.A.
CS Pathology/Laboratory Medicine Dept., Emory University,Atlanta, GA 30322, United States
SO AIDS Research and Human Retroviruses, (1994) 10/SUPPL. 2 (S95-S98). ISSN: 0889-2229 CODEN: ARHRE7
CY United States
DT Journal; Conference Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB Nonionic block copolymer adjuvants typically induce high-titer, long-lasting antibody responses, cell-mediated immunity, CTLs, and modulate the isotype and specificity of antibody. Their primary activity is modulation of hydrophobic adhesive interactions. The copolymers adhere to lipids, promote retention of protein **antigen** to surfaces, activate complement, and induce expression of class II (IA) on macrophages. They produce a concentrated surface matrix of **antigen** and activated host mediators that facilitates **antigen** presentation to cells of the immune system. The copolymer adjuvants act synergistically with multiple MDP and LPS preparations to increase total titers, especially those of the IgG(2a) and IgG(2b) isotypes. A surprising discovery was that they influence the specificity of antibody by at least two mechanisms. Saline formulations and oil-in-water (o/w) emulsions induced more antibody against labile, conformationally dependent epitopes on the surface of particles than water-in-oil (w/o) emulsions. Finally, we found that very large copolymers are able to stabilize water-in-oil-in-water (w/o/w) or multiple emulsions that can protect **antigen** during passage through the upper GI tract. They are therefore attractive vehicles for oral delivery of vaccines.

L16 ANSWER 49 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 93219674 EMBASE
DN 1993219674
TI Vaccine delivery systems: Potential methods for use in antifertility vaccines.
AU Stevens V.C.
CS Department of Obstetrics/Gynecology, Ohio State University, 1654 Upham Drive,Columbus, OH 43210, United States
SO American Journal of Reproductive Immunology, (1993) 29/3 (176-188). ISSN: 8755-8920 CODEN: AAJID6
CY Denmark
DT Journal; General Review
FS 010 Obstetrics and Gynecology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English

L16 ANSWER 50 OF 61 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 93031493 EMBASE
DN 1993031493
TI Novel vaccination strategies for the control of mucosal infection.
AU Husband A.J.
CS Department of Veterinary Pathology, University of Sydney,Sydney, NSW 2006, Australia
SO Vaccine, (1993) 11/2 (107-112).

ISSN: 0264-410X CODEN: VACCDE
CY United Kingdom
DT Journal; Conference Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB Eniteric disease remains one of the greatest causes of mortality and morbidity in both hiuman and veterinary species. There has been a remarkable lack of success in vaccination to control mucosal disease and it is therefore apparent that novel strategies are required to achieve effective mucosal immunity. Basic studies described in this paper have addressed problems associated with **antigen** handling and the induction of an immune response in the intestine, and the subsequent dissemination of effector cells and molecules to intestinal and extra-intestinal submucosal regions. Effective induction of IgA responses is dependent on T-cell help and requires cognate interactions between T cells and B cells within organized gut-associated lymphoid tissue (GALT). The delivery of an IgA antibody response to mucosal sites is also a T cell dependent but **antigen** driven process. The normal route by which **antigen** is taken up by GALT is via the epithelial surface but **antigen** presented in this way via villus epithelial cells generates predominantly a suppressor response. Strategies designed to overcome this effect included the use of powerful adjuvants (such as cholera toxin, muramyldipeptide and phorbol esters), the use of immunogenic carriers, or delivery via **liposomes**, microspheres or genetically engineered viral or bacterial vectors. Alternatively, the feasibility of accessing GALT via the serosal surface by administration of intraperitoneal **antigen** in oil **emulsion** has been explored and a vaccine formulation (Auspharm (patent pending)) has been developed which is suitable for IP delivery in commercial applications.

L16 ANSWER 51 OF 61 CAPLUS COPYRIGHT 2003 ACS
AN 1992:192476 CAPLUS
DN 116:192476
TI Vaccine compositions containing **liposomes**
IN Barchfeld, Gail L.; Ott, Gary; Van Nest, Gary A.
PA Chiron Corp., USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9200081	A1	19920109	WO 1991-US4532	19910625
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2086094	AA	19911230	CA 1991-2086094	19910625
AU 9183230	A1	19920123	AU 1991-83230	19910625
AU 654824	B2	19941124		
EP 489153	A1	19920610	EP 1991-914563	19910625
EP 489153	B1	19991013		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
BR 9106604	A	19930622	BR 1991-6604	19910625
JP 06504759	T2	19940602	JP 1991-513457	19910625
JP 2502234	B2	19960529		
HU 67055	A2	19950130	HU 1992-4136	19910625
AT 185486	E	19991015	AT 1991-914563	19910625
ES 2138588	T3	20000116	ES 1991-914563	19910625

	HU 220136	B	20011128	HU 1991-4136	19910625
	NO 9204858	A	19930225	NO 1992-4858	19921215
	US 5709879	A	19980120	US 1995-469444	19950606
PRAI	US 1990-546585	A	19900629		
	WO 1991-US4532	A	19910625		
	US 1991-722862	B1	19910628		
	US 1993-154160	B1	19931118		
	US 1994-308622	B1	19940919		

OS MARPAT 116:192476

AB A vaccine compn. comprises (1) a **liposome**-assocd. **antigen** and (2) an ion-in-water **emulsion** comprising a muramyl peptide, a metabolizable oil, and optionally an addnl. emulsifying agent. The 2 components of the **adjuvant** act together to produce high levels of immune response. Thus, fusogenic **liposomes** were prepd. e.g. from phosphatidylethanolamine and oleic acid (8:2) by reverse phase evapn. These **liposomes** were mixed with an oil-in-water **emulsion** contg. N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine 2-[1,2-dipalmitoyl-sn-glycero-3-(hydroxyphosphoryloxy)]ethylamide 400 .mu.g/mL, squalene 10, Tween 80 1, and Tetronic 1501 5% and with herpes simplex virus gD **antigen**. Immunization of goats with this combination gave a 3-fold higher antibody titer than immunization with only **emulsion** and gD2 **antigen**. Fusogenic and nonfusogenic **liposomes** were approx. equally effective. The antibody titer increased with increasing **antigen** assocn. with **liposomes**.

L16 ANSWER 52 OF 61 CAPLUS COPYRIGHT 2003 ACS

AN 1993:122811 CAPLUS

DN 118:122811

TI The control of the antibody isotype response to recombinant human immunodeficiency virus gp120 **antigen** by adjuvants

AU Bomford, R.; Stapleton, M.; Winsor, S.; McKnight, A.; Andronova, T.

CS Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK

SO AIDS Research and Human Retroviruses (1992), 8(10), 1765-71
CODEN: ARHRE7; ISSN: 0889-2229

DT Journal

LA English

AB Both saponin and muramyl dipeptide (MDP) formulated with a squalane-in-water **emulsion** of large particle size prepd. with a vortex mixer were superior to Al(OH)3 as adjuvants for HIV gp120 in mice. All the adjuvants induced IgG1 antibody, but saponin elicited the highest titers of IgG2a. The secretion of interleukin-5 (IL-5) and interferon-.gamma. (IFN.gamma.) by lymph node cells cultured in vitro with gp120 was studied. All the cultures secreted IL-5, but only those from saponin-immunized mice produced IFN.gamma., suggesting that saponin is capable of activating both the Th1 and Th2 T-cell subsets. The titers of neutralizing antibodies were low with both MDP and saponin, and they occurred in mice which were also pos. for antibodies against a V3 loop peptide. Glucosaminylmuramyl dipeptide (GMDP) which is less pyrogenic than MDP and a nonpyrogenic analog GMDPA, displayed equiv. **adjuvant** activity to MDP. The level and isotype compn. of antibodies induced by GMDP in combination with squalane emulsions depended on the dimension of the **emulsion** particles. With a large (2500 nm) particle size the response was confined to IgG1 in Balb/c mice, but when this was reduced to 150 nm by sonication the antibody response was increased and relatively high levels of IgG2a appeared in some mice.

L16 ANSWER 53 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1992:454887 BIOSIS

DN BA94:96287

TI ENHANCEMENT OF ANTIBODY RESPONSE OF TURKEYS TO TRIVALENT AVIAN INFLUENZA VACCINE BY POSITIVELY CHARGED **LIPOSOMAL** AVRIDINE **ADJUVANT**.

AU FATUNMBI O O; NEWMAN J A; SIVANANDAN V; HALVORSON D A
CS DEP. PATHOL., MICHIGAN STATE UNIV., EAST FEE, EAST LANSING, MICH. 48824, USA.
SO VACCINE, (1992) 10 (9), 623-626.
CODEN: VACCDE. ISSN: 0264-410X.
FS BA; OLD
LA English
AB Trivalent avian influenza (AIV) antigens (H4N8, H5N2 and H7N3), mixed with positively charged, negatively charged and neutral avridine-containing **liposomes**, and oil-**emulsion** were subcutaneously administered to 6-week-old turkeys. Charged **liposomal** avridine **adjuvant**, either positive or negative, produced a better antibody response than uncharged **liposomal** avridine or oil-**emulsion** adjuvants when used in a trivalent avian influenza vaccine. The antibody response to the different antigens was generally greater to the positively charged adjuvanted vaccine compared with the negatively or neutral charged or oil-**emulsion** adjuvanted vaccines and these differences were significant ($p < 0.05$) with the three antigens. The results suggest that the positively charged **liposomal** avridine plays a significant role as **adjuvant** to the AIV antigens.

L16 ANSWER 54 OF 61 CAPLUS COPYRIGHT 2003 ACS
AN 1991:49557 CAPLUS
DN 114:49557
TI Vaccine composition to stimulate IgA response in pigs
IN Husband, Alan James
PA Auspharm International Ltd., Australia
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9007935	A1	19900726	WO 1990-AU14	19900119
	W: AU, CA, FI, JP, NO, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	AU 9049599	A1	19900813	AU 1990-49599	19900119
	AU 638970	B2	19930715		
	EP 454735	A1	19911106	EP 1990-902112	19900119
	EP 454735	B1	19960522		
	R: DE, DK, FR, GB, NL				
	ZA 9000474	A	19901031	ZA 1990-474	19900123
PRAI	AU 1989-2368		19890123		
	WO 1990-AU14		19900119		

AB The title compn. for i.p. administration, comprises an antigenically active substance in a vegetable oil vehicle and, optionally, an **adjuvant**. In particular, vaccine compns. are provided for stimulation of a protective immune response against post-weaning enteritis and enzootic pneumonia in pigs. Thus, whereas ovalbumin given i.p. without **adjuvant** or vehicle produced virtually no anti-ovalbumin-contg.-cell (AOCC) response, ovalbumin with heat-killed Mycobacterium bivis in vegetable oil **emulsion** produced an AOCC response equiv. in magnitude to that obsd. with ovalbumin with Freund's complete **adjuvant**, but with an elevated proportion of AOCC of the IgA isotype. Pigs receiving vegetable oil-contg. vaccine produced an AOCC response which was not as great in pigs receiving ovalbumin with Freund's complete **adjuvant**, but had an equiv. IgA component. All pigs receiving Freund's complete **adjuvant**-contg. vaccine developed lesions and adhesions in the peritoneal cavity, but pigs receiving the vegetable oil-contg. vaccine had no lesion and no abnormalities detected at post mortem exam. Vaccination of pigs against

challenge by e.g. Mycoplasma hyopneumoniae is described.

L16 ANSWER 55 OF 61 MEDLINE DUPLICATE 14
AN 92182252 MEDLINE
DN 92182252 PubMed ID: 1966859
TI **Adjuvant** formulations and their mode of action.
AU Allison A C; Byars N E
CS Syntech Research, Palo Alto, CA 94304.
SO SEMINARS IN IMMUNOLOGY, (1990 Sep) 2 (5) 369-74.
Journal code: 9009458. ISSN: 1044-5323.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199204
ED Entered STN: 19920424
Last Updated on STN: 19970203
Entered Medline: 19920415
AB We have developed an **adjuvant** formulation (SAF) consisting of a synthetic muramyl dipeptide analogue (N-acetylmuramyl-L-threonyl-D-isoglutamine) in a squalane-Pluronic polymer **emulsion**. Used with a variety of antigens SAF elicits cell-mediated immunity and antibodies of protective isotypes (IgG2a in the mouse). SAF augments responses to influenza virus haemagglutinin and hepatitis B virus surface **antigen**. Vaccines using SAF have protected guinea pigs against genital herpes simplex virus infections and subhuman primates against Epstein-Barr virus and simian immunodeficiency virus infections. Properties of SAF are compared with those of other adjuvants, including lipopolysaccharide analogs, ISCOMs and **liposomes**.

L16 ANSWER 56 OF 61 CAPLUS COPYRIGHT 2003 ACS
AN 1989:205260 CAPLUS
DN 110:205260
TI Enhancement of humoral immune responses against viral vaccines by a non-pyrogenic 6-O-acyl-muramyldipeptide and synthetic low toxicity analogs of lipid A
AU Tsujimoto, Masachika; Kotani, Shozo; Okunaga, Takafumi; Kubo, Takao; Takada, Haruhiko; Kubo, Takasi; Shiba, Tetsuo; Kusumoto, Shoichi; Takahashi, Takashi; et al.
CS Dent. Sch., Osaka Univ., Osaka, 565, Japan
SO Vaccine (1989), 7(1), 39-48
CODEN: VACCDE; ISSN: 0264-410X
DT Journal
LA English
AB 6-O-Acyl derivs. of N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP) and synthetic, low toxicity lipid-A analogs were examd. for their ability to enhance the potency of current viral vaccines. 6-O-(2-Tetradecylhexadecanoyl)-MDP (B30-MDP) in non-irritative vehicles such as physiol. saline, phosphate-buffered saline (PBS), squalene-PBS **emulsion**, Intralipid or **liposomes**, stimulated the primary and secondary antibody prodn. of guinea-pigs against influenza split or subunit vaccine and inactivated hepatitis B virus surface (HBs) **antigen**. Mice seemed less responsive to the adjuvanticity of B30-MDP than guinea-pigs. Two low toxicity lipid A analogs, acylated .beta.(1-6)-D-glucosamine disaccharide bisphosphates (which do not have amide-bound or ester-bound 3-acyloxyacyl groups unlike fully toxic Escherichia coli-type lipid A), caused enhanced antibody responses, primary or secondary, when administered to mice by incorporation into **liposomes** with inactivated HBs **antigen**.

L16 ANSWER 57 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 15
AN 1986:439347 BIOSIS

DN BA82:105535
TI **ADJUVANT** ACTIVITY OF 6-O ACYLMURAMYLDIPEPTIDES TO ENHANCE PRIMARY CELLULAR AND HUMORAL IMMUNE RESPONSES IN GUINEA-PIGS ADAPTABILITY TO VARIOUS VEHICLES AND PYROGENICITY.
AU TSUJIMOTO M; KOTANI S; KINOSHITA F; KANOH S; SHIBA T; KUSUMOTO S
CS DEP. MICROBIOL. AND ORAL MICROBIOL., OSAKA UNIV. DENTAL SCH., 1-8 YAMADAOKA, SUITA, OSAKA 565, JPN.
SO INFECT IMMUN, (1986) 53 (3), 511-516.
CODEN: INFIBR. ISSN: 0019-9567.
FS BA; OLD
LA English
AB Thirteen 6-O-acyl-N-acetylmuramyl-L-alanyl-D-isoglutamines (6-O-acyl-MDPs), including four inactive D-isoasparagine and L-isoglutamine analogs, were tested for their pyrogenicity and immunopotentiating activity to stimulate primary humoral and cellular immune responses in guinea pigs to a model protein **antigen**, ovalbumin, when administered in various vehicles. Among them, derivatives whose muramic acid residue was substituted by .alpha.-branched (and .beta.-hydroxylated) higher fatty acids at the carbon-6 position, especially 6-O-(2-tetradecylhexadecanoyl)-MDP (B3O-MDP) and, to a lesser extent, 6-O-(3-hydroxy-2-docosylhexacosanoyl)-MDP (BH48-MDP) and its L-serine analog [BH48-MDP(L-Ser)], were found to exert strong **adjuvant** activity in both the induction of delayed-type hypersensitivity and the stimulation of circulating precipitating antibody levels when combined with nonirritating vehicles (**liposomes**, squalene-in-water **emulsion**, and phosphate-buffered saline). These vehicles did not efficiently support the **adjuvant** activity of MDP, the parent molecule of the above lipophilic derivatives. Pyrogenicity tests showed that introduction of .alpha.-branched higher fatty acid groups but not of straight, long-chain fatty acids at the 6-position of the muramic acid residue resulted in marked decrease of the pyrogenicity inherent to MDP via intravenous administration.

L16 ANSWER 58 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 16
AN 1984:226460 BIOSIS
DN BA77:59444
TI ORAL ADJUVANTS ENHANCE IMMUNO GLOBULIN A RESPONSES TO STREPTOCOCCUS-MUTANS.
AU MICHALEK S M; MORISAKI I; GREGORY R L; KIYONO H; HAMADA S; MCGHEE J R
CS DEP. MICROBIOL., INST. DENT. RES., UNIV. ALABAMA BIRMINGHAM, UNIV. STN., BIRMINGHAM, ALA. 35294, USA.
SO MOL IMMUNOL, (1983) 20 (9), 1009-1018.
CODEN: MOIMD5. ISSN: 0161-5890.
FS BA; OLD
LA English
AB The induction of immune responses to orally-administered trinitrophenyl (TNP)-haptenated S. mutans or its cell wall components and enhancement of immune responses with oral adjuvants was studied in high IgA responsive C3H/HeJ mice and in gnotobiotic rats. Gastric intubation of TNP-S. mutans to LPS [lipopolysaccharide] non-responsive C3H/HeJ or syngeneic, LPS responsive C3H/HeN mice induced IgA responses as determined by measuring splenic plaque-forming cell (PFC) responses and IgA anti-TNP antibodies in serum, saliva and urine. Higher IgA responses always occurred in C3H/HeJ mice given oral S. mutans **antigen** than similarly treated C3H/HeN animals. Oral administration of the adjuvants concanavalin A or S. mutans cell wall peptidoglycan (PG) with **antigen** resulted in augmented IgA responses, especially in C3H/HeJ mice. Oral administration of muramyl dipeptide (MDP) with **antigen** boosted anti-TNP responses in C3H/HeN, but not in C3H/HeJ, mice. Gnotobiotic rats given S. mutans whole cells (WC) or purified cell walls (CW) by the oral route exhibited a salivary IgA immune response which was potentiated > 2-fold when **antigen** was given with PG or MDP. In other studies, S. mutans WC

or CW **antigen** in water-oil-water (wow) **emulsion** or **liposomes** was administered by gastric intubation to rats. Significant salivary IgA responses were induced with these **antigen** -**adjuvant** preparations. Although rats given S. mutans WC or CW were protected from S. mutans challenge, the greatest degree of caries immunity was obtained in animals which received **antigen** and **adjuvant** and which exhibited significant salivary IgA antibody levels. In preliminary studies, it was observed that local injection of rats in the salivary gland region with a ribosomal preparation from S. mutans resulted in a significant salivary IgA response and caries immunity. The potential for soluble and lipid carrier adjuvants in oral vaccines for induction of protective antibodies to S. mutans is discussed.

L16 ANSWER 59 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 17

AN 1984:235916 BIOSIS

DN BA77:68900

TI **LIPOSOMES** AS A TOOL TO STUDY THE ROLE OF MEMBRANE PRESENTATION IN THE IMMUNOGENICITY OF A MURINE LEUKEMIA VIRUS RELATED TUMOR **ANTIGEN**.

AU GERLIER D; BAKOUCHE Q; DORE J F

CS INSERM U.218, CENTRE LEON BERARD, 69373 LYON CEDEX 2, FR.

SO J IMMUNOL, (1983) 131 (1), 485-490.
CODEN: JOIMA3. ISSN: 0022-1767.

FS BA; OLD

LA English

AB The immunogeneicity of a tumor cell surface-associated **antigen** is closely related to its presentation; usually the **antigen** that is presented on the cell membrane is a better immunogen than the **antigen** in soluble form. The immunogenicity of the Gross virus cell surface **antigen** GCSAa was studied in a syngeneic rat lymphoma model. Two injections of irradiated Gross virus-induced (C58NT)D lymphoma cells into W/Fu rats induced a high antibody response against GCSAa. Crude plasma membranes prepared from (C58NT)D cells could also induce a good anti-GCSAa antibody response when mixed with complete Freund **adjuvant** (CFA) and injected, whereas soluble GCSAa from the cytosol was a poor immunogen. To investigate the requirement for GCSAa to be associated with cell membranes to elicit an effective antibody response, soluble GCSAa prepared from the cytosol of (C58NT)D cells was incorporated into multilamellar **liposomes** made of dipalmitoyl phosphatidylcholine, cholesterol and dicetylphosphate in 7:2:1 molar ratio, and was used as immunogen. High antibody responses specific to GCSAa were obtained, but **emulsion** of the **liposome** preparation in CFA was also required. Because CFA could be replaced by incomplete Freund **adjuvant** but not by live BCG microorganisms, CFA was tentatively replaced by the addition to the **liposome** preparation of either a powerful chemotactic tripeptide, f-Met-Leu-Phe, or lipid A, or muramyldipeptide. In most of the experiments, the **liposome** preparation failed to show a higher immunogenicity than that of the soluble **antigen**. Alternatively, when the **liposome** preparation was incubated in vitro with peritoneal exudate cells before its injection into syngenic rats without any **adjuvant**, high antibody responses were observed in the animals. No significant antibody response was obtained in rats that also received either peritoneal exudate cells that were previously incubated with soluble **antigen**, or spleen cells that were depleted in adherent cells and previously incubated with the **antigen** preparations. The role of **liposome** presentation of GCSAa in the expression of its immunogenicity was also studied. The requirement for a constitutive association of GCSAa with **liposomes** was confirmed because injection of the soluble **antigen** mixed with preformed **liposomes** and emulsified in CFA did not induce a significant antibody response. The lipidic lamellae were separate from the aqueous

phase after mechanical disruption of the **liposome**-GCSAa preparation, and were used as immunogen: GCSAa associated with the lipidic lamellae was as immunogenic as the intact **liposome**-GCSAa preparation. The results strongly suggest the increase in GCSAa immunogenicity by **liposomes** results from a rapid in vivo recognition of unaltered **liposomes** by macrophages and is related to the presentation of the **antigen** in a membrane-like structure.

L16 ANSWER 60 OF 61 CAPLUS COPYRIGHT 2003 ACS
AN 1979:85053 CAPLUS
DN 90:85053
TI The immunoadjuvant activities of bacterial cell wall components with special reference to the effects of administration with various vehicles
AU Kinoshita, Fumio
CS 2nd Dep. Oral Surg., Osaka Univ. Dent. Sch., Osaka, Japan
SO Osaka Daigaku Shigaku Zasshi (1978), 23(1), 141-57
CODEN: ODSZA2; ISSN: 0473-4629
DT Journal
LA Japanese
AB Studies were made to evaluate the immune **adjuvant** activities of either synthetic N-acetylmuramyl-L-alanyl-D-isoglutamine (I) or bacterial cell wall peptidoglycan-subunit monomer, dimer, and polymer, administered to guinea pigs in various vehicles with ovalbumin as a test **antigen**. The following were satisfactory in manifestation of the activities of test adjuvants to induce a delayed-type hypersensitivity and to stimulate circulating antibody prodn., with tolerably weak local injurious effects: intra-footpad or i.p. injection of the above adjuvants as water-in-oil **emulsion** or double **emulsion** made of squalane; intra-footpad or i.p. injection of 6-o-lauroyl-, 6-o-stearoyl-, and 6-o-docosanoyl-I as **liposomes**; i.p. injection of 6-o-docosanoyl- and 6-o-(2-tetradecylhexadecanoyl)-I suspended in phosphate-buffered saline.

L16 ANSWER 61 OF 61 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1978:208949 BIOSIS
DN BA66:21446
TI IMMUNO **ADJUVANT** ACTIVITIES OF SYNTHETIC 6-O ACYL-N-ACETYLMURAMYL-L-ALANYL-D ISO GLUTAMINE WITH SPECIAL REFERENCE TO THE EFFECT OF ITS ADMINISTRATION WITH **LIPOSOMES**.
AU KOTANI S; KINOSHITA F; MORISAKI I; SHIMONO T; OKUNAGA T; TAKADA H; TSUJIMOTO M; WATANABE Y; KATO K; ET AL.
CS DEP. MICROBIOL., OSAKA UNIV. DEN. SCH., JOAN, KITA, OSAKA, JPN.
SO BIKEN J, (1977 (RECD 1978)) 20 (3-4), 95-104.
CODEN: BKNJA5. ISSN: 0006-2324.
FS BA; OLD
LA English
AB Addition of a lauroyl, stearoyl or docosanoyl group to the primary hydroxy group at the C-6 position of N-acetylmuramyl-L-alanyl-D-isoglutamine [NAMAI, the minimum structure required for the **adjuvant** activity of bacterial cell walls] gave lipophilic derivatives that had definite adjuvancies in induction of delayed-type hypersensitivity and enhancement of antibody production against a test protein **antigen**, ovalbumin, when administered to guinea pigs as **liposomes**, i.e., without mineral oil. When administered as mineral oil-in-water **emulsion**, including Ribi-type emulsions, rather than as water-in-mineral oil emulsions, NAMAI and its 6-O-acyl derivatives showed only weak immunoadjuvancies.